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| (21) International Application Number: PCT/US99/25044 (22) International Filing Date: 25 October 1999 (25.10.99) (30) Priority Data: 60/105,371 23 October 1998 (23.10.98) US 09/428,082 22 October 1999 (22.10.99) US (71) Applicant: AMGEN INC. [US/US]; One Amgen Center Drive, Thousand Oaks, CA 91320-1799 (US). (72) Inventors: FEIGE, Ulrich; 3117 Deer Valley Avenue, Newbury Park, CA 91320 (US). LIU, Chuan-Fa; 1425 Clover Creek Drive, Longmont, CO 80503 (US). CHEETHAM, Janet; 1695 East Valley Road, Montecito, CA 93108 (US). BOONE, Thomas, Charles; 3010 Deer Valley Avenue, Newbury Park, CA 91320 (US). (74) Agents: ODRE, Steven, M. et al.; Amgen, Inc., One Amgen Center Drive, Thousand Oaks, CA 91320-1799 (US). | | (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i> |
| (54) Title: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS (57) Abstract <p>The present invention concerns fusion of Fc domains with biologically active peptides and a process for preparing pharmaceutical agents using biologically active peptides. In this invention, pharmacologically active compounds are prepared by a process comprising: a) selecting at least one peptide that modulates the activity of a protein of interest; and b) preparing a pharmacologic agent comprising an Fc domain covalently linked to at least one amino acid of the selected peptide. Linkage to the vehicle increases the half-life of the peptide, which otherwise would be quickly degraded <i>in vivo</i>. The preferred vehicle is an Fc domain. The peptide is preferably selected by phage display, <i>E. coli</i> display, ribosome display, RNA-peptide screening, or chemical-peptide screening.</p> | | |

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Modified Peptides as Therapeutic Agents

Background of the Invention

Recombinant proteins are an emerging class of therapeutic agents.

5 Such recombinant therapeutics have engendered advances in protein formulation and chemical modification. Such modifications can protect therapeutic proteins, primarily by blocking their exposure to proteolytic enzymes. Protein modifications may also increase the therapeutic protein's stability, circulation time, and biological activity. A review
10 article describing protein modification and fusion proteins is Francis (1992), Focus on Growth Factors 3:4-10 (Mediscript, London), which is hereby incorporated by reference.

One useful modification is combination with the "Fc" domain of an antibody. Antibodies comprise two functionally independent parts, a
15 variable domain known as "Fab", which binds antigen, and a constant domain known as "Fc", which links to such effector functions as complement activation and attack by phagocytic cells. An Fc has a long serum half-life, whereas an Fab is short-lived. Capon et al. (1989), Nature 337: 525-31. When constructed together with a therapeutic protein, an Fc
20 domain can provide longer half-life or incorporate such functions as Fc receptor binding, protein A binding, complement fixation and perhaps even placental transfer. Id. Table 1 summarizes use of Fc fusions known in the art.

Table 1—Fc fusion with therapeutic proteins

| Form of Fc | Fusion partner | Therapeutic implications | Reference |
|--|-----------------------|---|--|
| IgG1 | N-terminus of CD30-L | Hodgkin's disease; anaplastic lymphoma; T-cell leukemia | U.S. Patent No. 5,480,981 |
| Murine Fc γ 2a | IL-10 | anti-inflammatory; transplant rejection | Zheng <i>et al.</i> (1995), <i>J. Immunol.</i> 154: 5590-600 |
| IgG1 | TNF receptor | septic shock | Fisher <i>et al.</i> (1996), <i>N. Engl. J. Med.</i> 334: 1697-1702; Van Zee, K. <i>et al.</i> (1996), <i>J. Immunol.</i> 156: 2221-30 |
| IgG, IgA, IgM, or IgE (excluding the first domain) | TNF receptor | inflammation, autoimmune disorders | U.S. Pat. No. 5,808,029, issued September 15, 1998 |
| IgG1 | CD4 receptor | AIDS | Capon <i>et al.</i> (1989), <i>Nature</i> 337: 525-31 |
| IgG1, IgG3 | N-terminus of IL-2 | anti-cancer, antiviral | Harvill <i>et al.</i> (1995), <i>Immunotech.</i> 1: 95-105 |
| IgG1 | C-terminus of OPG | osteoarthritis; bone density | WO 97/23614, published July 3, 1997 |
| IgG1 | N-terminus of leptin | anti-obesity | PCT/US 97/23183, filed December 11, 1997 |
| Human Ig Cy1 | CTLA-4 | autoimmune disorders | Linsley (1991), <i>J. Exp. Med.</i> 174:561-9 |

A much different approach to development of therapeutic agents is peptide library screening. The interaction of a protein ligand with its receptor often takes place at a relatively large interface. However, as demonstrated for human growth hormone and its receptor, only a few key residues at the interface contribute to most of the binding energy. Clackson *et al.* (1995), *Science* 267: 383-6. The bulk of the protein ligand merely displays the binding epitopes in the right topology or serves functions unrelated to binding. Thus, molecules of only "peptide" length (2 to 40 amino acids) can bind to the receptor protein of a given large protein ligand. Such peptides may mimic the bioactivity of the large protein ligand ("peptide agonists") or, through competitive binding, inhibit the bioactivity of the large protein ligand ("peptide antagonists").

Phage display peptide libraries have emerged as a powerful method in identifying such peptide agonists and antagonists. See, for example, Scott et al. (1990), Science 249: 386; Devlin et al. (1990), Science 249: 404; U.S. Pat. No. 5,223,409, issued June 29, 1993; U.S. Pat. No. 5,733,731, issued March 31, 1998; U.S. Pat. No. 5,498,530, issued March 12, 1996; U.S. Pat. No. 5,432,018, issued July 11, 1995; U.S. Pat. No. 5,338,665, issued August 16, 1994; U.S. Pat. No. 5,922,545, issued July 13, 1999; WO 96/40987, published December 19, 1996; and WO 98/15833, published April 16, 1998 (each of which is incorporated by reference). In such libraries, random peptide sequences are displayed by fusion with coat proteins of filamentous phage. Typically, the displayed peptides are affinity-eluted against an antibody-immobilized extracellular domain of a receptor. The retained phages may be enriched by successive rounds of affinity purification and repropagation. The best binding peptides may be sequenced to identify key residues within one or more structurally related families of peptides. See, e.g., Cwirla et al. (1997), Science 276: 1696-9, in which two distinct families were identified. The peptide sequences may also suggest which residues may be safely replaced by alanine scanning or by mutagenesis at the DNA level. Mutagenesis libraries may be created and screened to further optimize the sequence of the best binders. Lowman (1997), Ann. Rev. Biophys. Biomol. Struct. 26: 401-24.

Structural analysis of protein-protein interaction may also be used to suggest peptides that mimic the binding activity of large protein ligands. In such an analysis, the crystal structure may suggest the identity and relative orientation of critical residues of the large protein ligand, from which a peptide may be designed. See, e.g., Takasaki et al. (1997), Nature Biotech. 15: 1266-70. These analytical methods may also be used to investigate the interaction between a receptor protein and peptides

selected by phage display, which may suggest further modification of the peptides to increase binding affinity.

Other methods compete with phage display in peptide research. A peptide library can be fused to the carboxyl terminus of the lac repressor and expressed in E. coli. Another E. coli-based method allows display on the cell's outer membrane by fusion with a peptidoglycan-associated lipoprotein (PAL). Hereinafter, these and related methods are collectively referred to as "E. coli display." In another method, translation of random RNA is halted prior to ribosome release, resulting in a library of polypeptides with their associated RNA still attached. Hereinafter, this and related methods are collectively referred to as "ribosome display." Other methods employ chemical linkage of peptides to RNA; see, for example, Roberts & Szostak (1997), Proc. Natl. Acad. Sci. USA, 94: 12297-303. Hereinafter, this and related methods are collectively referred to as "RNA-peptide screening." Chemically derived peptide libraries have been developed in which peptides are immobilized on stable, non-biological materials, such as polyethylene rods or solvent-permeable resins. Another chemically derived peptide library uses photolithography to scan peptides immobilized on glass slides. Hereinafter, these and related methods are collectively referred to as "chemical-peptide screening." Chemical-peptide screening may be advantageous in that it allows use of D-amino acids and other unnatural analogues, as well as non-peptide elements. Both biological and chemical methods are reviewed in Wells & Lowman (1992), Curr. Opin. Biotechnol. 3: 355-62.

Conceptually, one may discover peptide mimetics of any protein using phage display and the other methods mentioned above. These methods have been used for epitope mapping, for identification of critical amino acids in protein-protein interactions, and as leads for the discovery of new therapeutic agents. E.g., Cortese et al. (1996), Curr. Opin. Biotech. 7:

616-21. Peptide libraries are now being used most often in immunological studies, such as epitope mapping. Kreeger (1996), The Scientist 10(13): 19-20.

5 Of particular interest here is use of peptide libraries and other techniques in the discovery of pharmacologically active peptides. A number of such peptides identified in the art are summarized in Table 2. The peptides are described in the listed publications, each of which is hereby incorporated by reference. The pharmacologic activity of the peptides is described, and in many instances is followed by a shorthand
10 term therefor in parentheses. Some of these peptides have been modified (e.g., to form C-terminally cross-linked dimers). Typically, peptide libraries were screened for binding to a receptor for a pharmacologically active protein (e.g., EPO receptor). In at least one instance (CTLA4), the peptide library was screened for binding to a monoclonal antibody.

Table 2—Pharmacologically active peptides

| Form of peptide | Binding partner/ protein of interest ^a | Pharmacologic activity | Reference |
|---------------------------------|--|--|--|
| intrapeptide disulfide-bonded | EPO receptor | EPO-mimetic | Wrighton <i>et al.</i> (1996), <i>Science</i> 273: 458-63; U.S. Pat. No. 5,773,569, issued June 30, 1998 to Wrighton <i>et al.</i> |
| C-terminally cross-linked dimer | EPO receptor | EPO-mimetic | Livnah <i>et al.</i> (1996), <i>Science</i> 273: 464-71; Wrighton <i>et al.</i> (1997), <i>Nature Biotechnology</i> 15: 1261-5; International patent application WO 96/40772, published Dec. 19, 1996 |
| linear | EPO receptor | EPO-mimetic | Naranda <i>et al.</i> (1999), <i>Proc. Natl. Acad. Sci. USA</i> , 96: 7569-74 |
| linear | c-Mpl | TPO-mimetic | Cwirla <i>et al.</i> (1997) <i>Science</i> 276: 1696-9; U.S. Pat. No. 5,869,451, issued Feb. 9, 1999; U.S. Pat. No. 5,932,946, issued Aug. 3, 1999 |
| C-terminally cross-linked dimer | c-Mpl | TPO-mimetic | Cwirla <i>et al.</i> (1997), <i>Science</i> 276: 1696-9 |
| disulfide-linked dimer | | stimulation of hematopoiesis ("G-CSF-mimetic") | Paukovits <i>et al.</i> (1984), <i>Hoppe-Seyler's Z. Physiol. Chem.</i> 365: 303-11; Laerum <i>et al.</i> (1988), <i>Exp. Hemat.</i> 16: 274-80 |
| alkylene-linked dimer | | G-CSF-mimetic | Bhatnagar <i>et al.</i> (1996), <i>J. Med. Chem.</i> 39: 3814-9; Cuthbertson <i>et al.</i> (1997), <i>J. Med. Chem.</i> 40: 2876-82; King <i>et al.</i> (1991), <i>Exp. Hematol.</i> 19:481; King <i>et al.</i> (1995), <i>Blood</i> 86 (Suppl. 1): 309a |
| linear | IL-1 receptor | inflammatory and autoimmune diseases ("IL-1 antagonist" or "IL-1ra-mimetic") | U.S. Pat. No. 5,608,035; U.S. Pat. No. 5,786,331; U.S. Pat. No. 5,880,096; Yanofsky <i>et al.</i> (1996), |

^a The protein listed in this column may be bound by the associated peptide (e.g., EPO receptor, IL-1 receptor) or mimicked by the associated peptide. The references listed for each clarify whether the molecule is bound by or mimicked by the peptides.

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| | | | Proc. Natl. Acad. Sci. 93: 7381-6; Akeson <i>et al.</i> (1996), <i>J. Biol. Chem.</i> 271: 30517-23; Wiekzorek <i>et al.</i> (1997), <i>Pol. J. Pharmacol.</i> 49: 107-17; Yanofsky (1996), <i>PNAs</i> , 93:7381-7386. |
| linear | Facteur thymique serique (FTS) | stimulation of lymphocytes ("FTS-mimetic") | Inagaki-Ohara <i>et al.</i> (1996), <i>Cellular Immunol.</i> 171: 30-40; Yoshida (1984), <i>Int. J. Immunopharmacol.</i> 6:141-6. |
| intrapeptide disulfide bonded | CTLA4 MAb | CTLA4-mimetic | Fukumoto <i>et al.</i> (1998), <i>Nature Biotech.</i> 16: 267-70 |
| exocyclic | TNF- α receptor | TNF- α antagonist | Takasaki <i>et al.</i> (1997), <i>Nature Biotech.</i> 15:1266-70; WO 98/53842, published December 3, 1998 |
| linear | TNF- α receptor | TNF- α antagonist | Chirinos-Rojas (), <i>J. Imm.</i> , 5621-5626. |
| intrapeptide disulfide bonded | C3b | inhibition of complement activation; autoimmune diseases ("C3b-antagonist") | Sahu <i>et al.</i> (1996), <i>J. Immunol.</i> 157: 884-91; Morikis <i>et al.</i> (1998), <i>Protein Sci.</i> 7: 619-27 |
| linear | vinculin | cell adhesion processes—cell growth, differentiation, wound healing, tumor metastasis ("vinculin binding") | Adey <i>et al.</i> (1997), <i>Biochem. J.</i> 324: 523-8 |
| linear | C4 binding protein (C4BP) | anti-thrombotic | Linse <i>et al.</i> (1997), <i>J. Biol. Chem.</i> 272: 14658-65 |
| linear | urokinase receptor | processes associated with urokinase interaction with its receptor (e.g., angiogenesis, tumor cell invasion and metastasis); ("UKR antagonist") | Goodson <i>et al.</i> (1994), <i>Proc. Natl. Acad. Sci.</i> 91: 7129-33; International application WO 97/35969, published October 2, 1997 |
| linear | Mdm2, Hdm2 | Inhibition of inactivation of p53 mediated by Mdm2 or hdm2; anti-tumor ("Mdm/hdm antagonist") | Picksley <i>et al.</i> (1994), <i>Oncogene</i> 9: 2523-9; Bottger <i>et al.</i> (1997) <i>J. Mol. Biol.</i> 269: 744-56; Bottger <i>et al.</i> (1996), <i>Oncogene</i> 13: 2141-7 |
| linear | p21 ^{WAF1} | anti-tumor by mimicking the activity of p21 ^{WAF1} | Batl <i>et al.</i> (1997), <i>Curr. Biol.</i> 7: 71-80 |
| linear | farnesyl | anti-cancer by preventing | Gibbs <i>et al.</i> (1994), <i>Cell</i> |

^b FTS is a thymic hormone mimicked by the molecule of this invention rather than a receptor bound by the molecule of this invention.

| | | | |
|----------------------|---------------------------------------|---|---|
| linear | transferase Ras effector domain | activation of ras oncogene anti-cancer by inhibiting biological function of the ras oncogene | 77:175-178 Moodie et al. (1994), <u>Trends Genet</u> 10: 44-48 Rodriguez et al. (1994), <u>Nature</u> 370:527-532 |
| linear | SH2/SH3 domains | anti-cancer by inhibiting tumor growth with activated tyrosine kinases | Pawson et al (1993), <u>Curr. Biol.</u> 3:434-432 Yu et al. (1994), <u>Cell</u> 76:933-945 |
| linear | p16 ^{INK4} | anti-cancer by mimicking activity of p16; e.g., inhibiting cyclin D-Cdk complex ("p16-mimetic") | Fåhræus et al. (1996), <u>Curr. Biol.</u> 6:84-91 |
| linear | Src, Lyn | inhibition of Mast cell activation, IgE-related conditions, type I hypersensitivity ("Mast cell antagonist") | Stauffer et al. (1997), <u>Biochem.</u> 36: 9388-94 |
| linear | Mast cell protease | treatment of inflammatory disorders mediated by release of tryptase-6 ("Mast cell protease inhibitors") | International application WO 98/33812, published August 6, 1998 |
| linear | SH3 domains | treatment of SH3- mediated disease states ("SH3 antagonist") | Rickles et al. (1994), <u>EMBO J.</u> 13: 5598-5604; Sparks et al. (1994), <u>J.</u> <u>Biol. Chem.</u> 269: 23853- 6; Sparks et al. (1996), <u>Proc. Natl. Acad. Sci.</u> 93: 1540-4 |
| linear | HBV core antigen (HBcAg) | treatment of HBV viral infections ("anti-HBV") | Dyson & Muray (1995), <u>Proc. Natl. Acad. Sci.</u> 92: 2194-8 |
| linear | selectins | neutrophil adhesion; inflammatory diseases ("selectin antagonist") | Martens et al. (1995), <u>J.</u> <u>Biol. Chem.</u> 270: 21129- 36; European patent application EP 0 714 912, published June 5, 1996 |
| linear, cyclized | calmodulin | calmodulin antagonist | Pierce et al. (1995), <u>Molec. Diversity</u> 1: 259- 65; Dedman et al. (1993), <u>J. Biol. Chem.</u> 268: 23025-30; Adey & Kay (1996), <u>Gene</u> 169: 133-4 |
| linear, cyclized- | integrins | tumor-homing; treatment for conditions related to integrin-mediated cellular events, including platelet aggregation, thrombosis, wound healing, osteoporosis, tissue repair, angiogenesis (e.g., | International applications WO 95/14714, published June 1, 1995; WO 97/08203, published March 6, 1997; WO 98/10795, published March 19, 1998; WO 99/24462, published May |

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| | | for treatment of cancer), and tumor invasion ("integrin-binding") | 20, 1999; Kraft <i>et al.</i> (1999), <i>J. Biol. Chem.</i> 274: 1979-1985 |
| cyclic, linear | fibronectin and extracellular matrix components of T cells and macrophages | treatment of inflammatory and autoimmune conditions | WO 98/09985, published March 12, 1998 |
| linear | somatostatin and cortistatin | treatment or prevention of hormone-producing tumors, acromegaly, giantism, dementia, gastric ulcer, tumor growth, inhibition of hormone secretion, modulation of sleep or neural activity | European patent application 0 911 393, published April 28, 1999 |
| linear | bacterial lipopolysac- charide | antibiotic; septic shock; disorders modulatable by CAP37 | U.S. Pat. No. 5,877,151, issued March 2, 1999 |
| linear or cyclic, including D- amino acids | pardaxin, mellitin | antipathogenic | WO 97/31019, published 28 August 1997 |
| linear, cyclic | VIP | impotence, neurodegenerative disorders | WO 97/40070, published October 30, 1997 |
| linear | CTLs | cancer | EP 0 770 624, published May 2, 1997 |
| linear | THF-gamma2 | | Burnstein (1988), <i>Biochem.</i> , 27:4066-71. |
| linear | Amylin | | Cooper (1987), <i>Proc.</i> <i>Natl. Acad. Sci.</i> , 84:8628-32. |
| linear | Adrenomedullin | | Kitamura (1993), <i>BBRC</i> , 192:553-60. |
| cyclic, linear | VEGF | anti-angiogenic; cancer, rheumatoid arthritis, diabetic retinopathy, psoriasis ("VEGF antagonist") | Fairbrother (1998), <i>Biochem.</i> , 37:17754- 17764. |
| cyclic | MMP | inflammation and autoimmune disorders; tumor growth ("MMP inhibitor") | Koivunen (1999), <i>Nature</i> <i>Biotech.</i> , 17:768-774. |
| | HGH fragment | | U.S. Pat. No. 5,869,452 |
| | Echistatin | inhibition of platelet aggregation | Gan (1988), <i>J. Biol.</i> <i>Chem.</i> , 263:19827-32. |
| linear | SLE autoantibody | SLE | WO 96/30057, published October 3, 1996 |
| | GD1alpha | suppression of tumor metastasis | Ishikawa <i>et al.</i> (1998), <i>FEBS Lett.</i> 441 (1): 20-4 |
| | antiphospholipid | endothelial cell activation , | Blank <i>et al.</i> (1999), <i>Proc.</i> |

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| | beta-2-glycoprotein-I (β 2GPI) antibodies | antiphospholipid syndrome (APS), thromboembolic phenomena, thrombocytopenia, and recurrent fetal loss | Natl. Acad. Sci. USA 96: 5164-8 |
| linear | T Cell Receptor beta chain | diabetes | WO 96/11214, published April 18, 1996 |

Peptides identified by peptide library screening have been regarded as "leads" in development of therapeutic agents rather than as therapeutic agents themselves. Like other proteins and peptides, they would be rapidly removed in vivo either by renal filtration, cellular clearance mechanisms in the reticuloendothelial system, or proteolytic degradation. Francis (1992), Focus on Growth Factors 3: 4-11. As a result, the art presently uses the identified peptides to validate drug targets or as scaffolds for design of organic compounds that might not have been as easily or as quickly identified through chemical library screening. Lowman (1997), Ann. Rev. Biophys. Biomol. Struct. 26: 401-24; Kay et al. (1998), Drug Disc. Today 3: 370-8. The art would benefit from a process by which such peptides could more readily yield therapeutic agents.

Summary of the Invention

The present invention concerns a process by which the in vivo half-life of one or more biologically active peptides is increased by fusion with a vehicle. In this invention, pharmacologically active compounds are prepared by a process comprising:

- a) selecting at least one peptide that modulates the activity of a protein of interest; and
- b) preparing a pharmacologic agent comprising at least one vehicle covalently linked to at least one amino acid sequence of the selected peptide.

The preferred vehicle is an Fc domain. The peptides screened in step (a) are preferably expressed in a phage display library. The vehicle and the

peptide may be linked through the N- or C-terminus of the peptide or the vehicle, as described further below. Derivatives of the above compounds (described below) are also encompassed by this invention.

5 The compounds of this invention may be prepared by standard synthetic methods, recombinant DNA techniques, or any other methods of preparing peptides and fusion proteins. Compounds of this invention that encompass non-peptide portions may be synthesized by standard organic chemistry reactions, in addition to standard peptide chemistry reactions when applicable.

10 The primary use contemplated is as therapeutic or prophylactic agents. The vehicle-linked peptide may have activity comparable to—or even greater than—the natural ligand mimicked by the peptide. In addition, certain natural ligand-based therapeutic agents might induce antibodies against the patient's own endogenous ligand; the vehicle-linked
15 peptide avoids this pitfall by having little or typically no sequence identity with the natural ligand.

Although mostly contemplated as therapeutic agents, compounds of this invention may also be useful in screening for such agents. For example, one could use an Fc-peptide (e.g., Fc-SH2 domain peptide) in an
20 assay employing anti-Fc coated plates. The vehicle, especially Fc, may make insoluble peptides soluble and thus useful in a number of assays.

The compounds of this invention may be used for therapeutic or prophylactic purposes by formulating them with appropriate pharmaceutical carrier materials and administering an effective amount to
25 a patient, such as a human (or other mammal) in need thereof. Other related aspects are also included in the instant invention.

Numerous additional aspects and advantages of the present invention will become apparent upon consideration of the figures and detailed description of the invention.

Brief Description of the Figures

Figure 1 shows a schematic representation of an exemplary process of the invention. In this preferred process, the vehicle is an Fc domain, which is linked to the peptide covalently by expression from a DNA construct encoding both the Fc domain and the peptide. As noted in
5 Figure 1, the Fc domains spontaneously form a dimer in this process.

Figure 2 shows exemplary Fc dimers that may be derived from an IgG1 antibody. "Fc" in the figure represents any of the Fc variants within the meaning of "Fc domain" herein. "X¹" and "X²" represent peptides or
10 linker-peptide combinations as defined hereinafter. The specific dimers are as follows:

A, D: Single disulfide-bonded dimers. IgG1 antibodies typically have two disulfide bonds at the hinge region between the constant and variable domains. The Fc domain in Figures 2A and 2D may be formed by
15 truncation between the two disulfide bond sites or by substitution of a cysteinyl residue with an unreactive residue (e.g., alanyl). In Figure 2A, the Fc domain is linked at the amino terminus of the peptides; in 2D, at the carboxyl terminus.

B, E: Doubly disulfide-bonded dimers. This Fc domain may be
20 formed by truncation of the parent antibody to retain both cysteinyl residues in the Fc domain chains or by expression from a construct including a sequence encoding such an Fc domain. In Figure 2B, the Fc domain is linked at the amino terminus of the peptides; in 2E, at the carboxyl terminus.

25 C, F: Noncovalent dimers. This Fc domain may be formed by elimination of the cysteinyl residues by either truncation or substitution. One may desire to eliminate the cysteinyl residues to avoid impurities formed by reaction of the cysteinyl residue with cysteinyl residues of other

proteins present in the host cell. The noncovalent bonding of the Fc domains is sufficient to hold together the dimer.

Other dimers may be formed by using Fc domains derived from different types of antibodies (e.g., IgG2, IgM).

5 Figure 3 shows the structure of preferred compounds of the invention that feature tandem repeats of the pharmacologically active peptide. Figure 3A shows a single chain molecule and may also represent the DNA construct for the molecule. Figure 3B shows a dimer in which the linker-peptide portion is present on only one chain of the dimer. Figure 3C
10 shows a dimer having the peptide portion on both chains. The dimer of Figure 3C will form spontaneously in certain host cells upon expression of a DNA construct encoding the single chain shown in Figure 3A. In other host cells, the cells could be placed in conditions favoring formation of dimers or the dimers can be formed in vitro.

15 Figure 4 shows exemplary nucleic acid and amino acid sequences (SEQ ID NOS: 1 and 2, respectively) of human IgG1 Fc that may be used in this invention.

 Figure 5 shows a synthetic scheme for the preparation of PEGylated peptide 19 (SEQ ID NO: 3).

20 Figure 6 shows a synthetic scheme for the preparation of PEGylated peptide 20 (SEQ ID NO: 4).

 Figure 7 shows the nucleotide and amino acid sequences (SEQ ID NOS: 5 and 6, respectively) of the molecule identified as "Fc-TMP" in Example 2 hereinafter.

25 Figure 8 shows the nucleotide and amino acid sequences (SEQ. ID. NOS: 7 and 8, respectively) of the molecule identified as "Fc-TMP-TMP" in Example 2 hereinafter.

Figure 9 shows the nucleotide and amino acid sequences (SEQ. ID. NOS: 9 and 10, respectively) of the molecule identified as "TMP-TMP-Fc" in Example 2 hereinafter.

Figure 10 shows the nucleotide and amino acid sequences (SEQ. ID. NOS: 11 and 12, respectively) of the molecule identified as "TMP-Fc" in Example 2 hereinafter.

Figure 11 shows the number of platelets generated in vivo in normal female BDF1 mice treated with one 100 µg/kg bolus injection of various compounds, with the terms defined as follows.

10 PEG-MGDF: 20 kD average molecular weight PEG attached by reductive amination to the N-terminal amino group of amino acids 1-163 of native human TPO, which is expressed in E. coli (so that it is not glycosylated);

15 TMP: the TPO-mimetic peptide having the amino acid sequence IEGPTLRQWLAARA (SEQ ID NO: 13);

TMP-TMP: the TPO-mimetic peptide having the amino acid sequence IEGPTLRQWLAARA-GGGGGGGG-IEGPTLRQWLAARA (SEQ ID NO: 14);

20 PEG-TMP-TMP: the peptide of SEQ ID NO: 14, wherein the PEG group is a 5 kD average molecular weight PEG attached as shown in Figure 6;

Fc-TMP-TMP: the compound of SEQ ID NO: 8 (Figure 8) dimerized with an identical second monomer (i.e., Cys residues 7 and 10 are bound to the corresponding Cys residues in the second monomer to form a dimer, as shown in Figure 2); and

25 TMP-TMP-Fc is the compound of SEQ ID NO: 10 (Figure 9) dimerized in the same way as TMP-TMP-Fc except that the Fc domain is attached at the C-terminal end rather than the N-terminal end of the TMP-TMP peptide.

Figure 12 shows the number of platelets generated in vivo in normal BDF1 mice treated with various compounds delivered via implanted osmotic pumps over a 7-day period. The compounds are as defined for Figure 7.

5 Figure 13 shows the nucleotide and amino acid sequences (SEQ. ID. NOS: 15 and 16, respectively) of the molecule identified as "Fc-EMP" in Example 3 hereinafter.

Figure 14 shows the nucleotide and amino acid sequences (SEQ ID NOS: 17 and 18, respectively) of the molecule identified as "EMP-Fc" in
10 Example 3 hereinafter.

Figure 15 shows the nucleotide and amino acid sequences (SEQ ID NOS:19 and 20, respectively) of the molecule identified as "EMP-EMP-Fc" in Example 3 hereinafter.

Figure 16 shows the nucleotide and amino acid sequences (SEQ ID NOS: 21 and 22, respectively) of the molecule identified as "Fc-EMP-EMP"
15 in Example 3 hereinafter.

Figures 17A and 17B show the DNA sequence (SEQ ID NO: 23) inserted into pCFM1656 between the unique AatII (position #4364 in pCFM1656) and SacII (position #4585 in pCFM1656) restriction sites to
20 form expression plasmid pAMG21 (ATCC accession no. 98113).

Figure 18A shows the hemoglobin, red blood cells, and hematocrit generated in vivo in normal female BDF1 mice treated with one 100 µg/kg bolus injection of various compounds. Figure 18B shows the same results with mice treated with 100 µg/kg per day delivered ~~the same dose~~ by 7-
25 day micro-osmotic pump with the EMPs delivered at 100 µg/kg, rhEPO at 30U/mouse. (In both experiments, neutrophils, lymphocytes, and platelets were unaffected.) In these figures, the terms are defined as follows.

Fc-EMP: the compound of SEQ ID NO: 16 (Figure 13) dimerized with an identical second monomer (i.e., Cys residues 7 and 10 are

bound to the corresponding Cys residues in the second monomer to form a dimer, as shown in Figure 2);

EMP-Fc: the compound of SEQ ID NO: 18 (Figure 14) dimerized in the same way as Fc-EMP except that the Fc domain is attached at the C-terminal end rather than the N-terminal end of the EMP peptide.

"EMP-EMP-Fc" refers to a tandem repeat of the same peptide (SEQ ID NO: 20) attached to the same Fc domain by the carboxyl terminus of the peptides. "Fc-EMP-EMP" refers to the same tandem repeat of the peptide but with the same Fc domain attached at the amino terminus of the tandem repeat. All molecules are expressed in E. coli and so are not glycosylated.

Figures 19A and 19B show the nucleotide and amino acid sequences (SEQ ID NOS: 1055 and 1056) of the Fc-TNF- α inhibitor fusion molecule described in Example 4 hereinafter.

Figures 20A and 20B show the nucleotide and amino acid sequences (SEQ ID NOS: 1057 and 1058) of the TNF- α inhibitor-Fc fusion molecule described in Example 4 hereinafter.

Figures 21A and 21B show the nucleotide and amino acid sequences (SEQ ID NOS: 1059 and 1060) of the Fc-IL-1 antagonist fusion molecule described in Example 5 hereinafter.

Figures 22A and 22B show the nucleotide and amino acid sequences (SEQ ID NOS: 1061 and 1062) of the IL-1 antagonist-Fc fusion molecule described in Example 5 hereinafter.

Figures 23A, 23B, and 23C show the nucleotide and amino acid sequences (SEQ ID NOS: 1063 and 1064) of the Fc-VEGF antagonist fusion molecule described in Example 6 hereinafter.

Figures 24A and 24B show the nucleotide and amino acid sequences (SEQ ID NOS: 1065 and 1066) of the VEGF antagonist-Fc fusion molecule described in Example 6 hereinafter.

Figures 25A and 25B show the nucleotide and amino acid sequences (SEQ ID NOS: 1067 and 1068) of the Fc-MMP inhibitor fusion molecule described in Example 7 hereinafter.

Figures 26A and 26B show the nucleotide and amino acid sequences (SEQ ID NOS: 1069 and 1070) of the MMP inhibitor-Fc fusion molecule described in Example 7 hereinafter.

Detailed Description of the Invention

Definition of Terms

The terms used throughout this specification are defined as follows, unless otherwise limited in specific instances.

The term "comprising" means that a compound may include additional amino acids on either or both of the N- or C- termini of the given sequence. Of course, these additional amino acids should not significantly interfere with the activity of the compound.

The term "vehicle" refers to a molecule that prevents degradation and/or increases half-life, reduces toxicity, reduces immunogenicity, or increases biological activity of a therapeutic protein. Exemplary vehicles include an Fc domain (which is preferred) as well as a linear polymer (e.g., polyethylene glycol (PEG), polylysine, dextran, etc.); a branched-chain polymer (see, for example, U.S. Patent No. 4,289,872 to Denkenwalter et al., issued September 15, 1981; 5,229,490 to Tam, issued July 20, 1993; WO 93/21259 by Frechet et al., published 28 October 1993); a lipid; a cholesterol group (such as a steroid); a carbohydrate or oligosaccharide; or any natural or synthetic protein, polypeptide or peptide that binds to a salvage receptor. Vehicles are further described hereinafter.

The term "native Fc" refers to molecule or sequence comprising the sequence of a non-antigen-binding fragment resulting from digestion of whole antibody, whether in monomeric or multimeric form. The original immunoglobulin source of the native Fc is preferably of human origin and
5 may be any of the immunoglobulins, although IgG1 and IgG2 are preferred. Native Fc's are made up of monomeric polypeptides that may be linked into dimeric or multimeric forms by covalent (i.e., disulfide bonds) and non-covalent association. The number of intermolecular disulfide bonds between monomeric subunits of native Fc molecules
10 ranges from 1 to 4 depending on class (e.g., IgG, IgA, IgE) or subclass (e.g., IgG1, IgG2, IgG3, IgA1, IgGA2). One example of a native Fc is a disulfide-bonded dimer resulting from papain digestion of an IgG (see Ellison *et al.* (1982), Nucleic Acids Res. 10: 4071-9). The term "native Fc" as used herein is generic to the monomeric, dimeric, and multimeric forms.

15 The term "Fc variant" refers to a molecule or sequence that is modified from a native Fc but still comprises a binding site for the salvage receptor, FcRn. International applications WO 97/34631 (published 25 September 1997) and WO 96/32478 describe exemplary Fc variants, as well as interaction with the salvage receptor, and are hereby incorporated
20 by reference. Thus, the term "Fc variant" comprises a molecule or sequence that is humanized from a non-human native Fc. Furthermore, a native Fc comprises sites that may be removed because they provide structural features or biological activity that are not required for the fusion molecules of the present invention. Thus, the term "Fc variant" comprises
25 a molecule or sequence that lacks one or more native Fc sites or residues that affect or are involved in (1) disulfide bond formation, (2) incompatibility with a selected host cell (3) N-terminal heterogeneity upon expression in a selected host cell, (4) glycosylation, (5) interaction with complement, (6) binding to an Fc receptor other than a salvage receptor, or

(7) antibody-dependent cellular cytotoxicity (ADCC). Fc variants are described in further detail hereinafter.

The term "Fc domain" encompasses native Fc and Fc variant molecules and sequences as defined above. As with Fc variants and native
5 Fc's, the term "Fc domain" includes molecules in monomeric or multimeric form, whether digested from whole antibody or produced by other means.

The term "multimer" as applied to Fc domains or molecules comprising Fc domains refers to molecules having two or more
10 polypeptide chains associated covalently, noncovalently, or by both covalent and non-covalent interactions. IgG molecules typically form dimers; IgM, pentamers; IgD, dimers; and IgA, monomers, dimers, trimers, or tetramers. Multimers may be formed by exploiting the sequence and resulting activity of the native Ig source of the Fc or by
15 derivatizing (as defined below) such a native Fc.

The term "dimer" as applied to Fc domains or molecules comprising Fc domains refers to molecules having two polypeptide chains associated covalently or non-covalently. Thus, exemplary dimers within the scope of this invention are as shown in Figure 2.

20 The terms "derivatizing" and "derivative" or "derivatized" comprise processes and resulting compounds respectively in which (1) the compound has a cyclic portion; for example, cross-linking between cysteinyl residues within the compound; (2) the compound is cross-linked or has a cross-linking site; for example, the compound has a cysteinyl
25 residue and thus forms cross-linked dimers in culture or in vivo; (3) one or more peptidyl linkage is replaced by a non-peptidyl linkage; (4) the N-terminus is replaced by $-NRR^1$, $-NRC(O)R^1$, $-NRC(O)OR^1$, $-NRS(O)_2R^1$, $-NHC(O)NHR$, a succinimide group, or substituted or unsubstituted benzyloxycarbonyl-NH-, wherein R and R^1 and the ring substituents are

as defined hereinafter; (5) the C-terminus is replaced by $-C(O)R^2$ or $-NR^3R^4$ wherein R^2 , R^3 and R^4 are as defined hereinafter; and (6) compounds in which individual amino acid moieties are modified through treatment with agents capable of reacting with selected side chains or terminal
5 residues. Derivatives are further described hereinafter.

The term "peptide" refers to molecules of 2 to 40 amino acids, with molecules of 3 to 20 amino acids preferred and those of 6 to 15 amino acids most preferred. Exemplary peptides may be randomly generated by any of the methods cited above, carried in a peptide library (e.g., a phage
10 display library), or derived by digestion of proteins.

The term "randomized" as used to refer to peptide sequences refers to fully random sequences (e.g., selected by phage display methods) and sequences in which one or more residues of a naturally occurring molecule is replaced by an amino acid residue not appearing in that position in the
15 naturally occurring molecule. Exemplary methods for identifying peptide sequences include phage display, *E. coli* display, ribosome display, RNA-peptide screening, chemical screening, and the like.

The term "pharmacologically active" means that a substance so described is determined to have activity that affects a medical parameter
20 (e.g., blood pressure, blood cell count, cholesterol level) or disease state (e.g., cancer, autoimmune disorders). Thus, pharmacologically active peptides comprise agonistic or mimetic and antagonistic peptides as defined below.

The terms "-mimetic peptide" and "-agonist peptide" refer to a
25 peptide having biological activity comparable to a protein (e.g., EPO, TPO, G-CSF) that interacts with a protein of interest. These terms further include peptides that indirectly mimic the activity of a protein of interest, such as by potentiating the effects of the natural ligand of the protein of interest; see, for example, the G-CSF-mimetic peptides listed in Tables 2

and 7. Thus, the term "EPO-mimetic peptide" comprises any peptides that can be identified or derived as described in Wrighton et al. (1996), Science 273: 458-63, Naranda et al. (1999), Proc. Natl. Acad. Sci. USA 96: 7569-74, or any other reference in Table 2 identified as having EPO-mimetic subject matter. Those of ordinary skill in the art appreciate that each of these references enables one to select different peptides than actually disclosed therein by following the disclosed procedures with different peptide libraries.

The term "TPO-mimetic peptide" comprises peptides that can be identified or derived as described in Cwirla et al. (1997), Science 276: 1696-9, U.S. Pat. Nos. 5,869,451 and 5,932,946 and any other reference in Table 2 identified as having TPO-mimetic subject matter, as well as the U.S. patent application, "Thrombopoietic Compounds," filed on even date herewith and hereby incorporated by reference. Those of ordinary skill in the art appreciate that each of these references enables one to select different peptides than actually disclosed therein by following the disclosed procedures with different peptide libraries.

The term "G-CSF-mimetic peptide" comprises any peptides that can be identified or described in Paukovits et al. (1984), Hoppe-Seylers Z. Physiol. Chem. 365: 303-11 or any of the references in Table 2 identified as having G-CSF-mimetic subject matter. Those of ordinary skill in the art appreciate that each of these references enables one to select different peptides than actually disclosed therein by following the disclosed procedures with different peptide libraries.

The term "CTLA4-mimetic peptide" comprises any peptides that can be identified or derived as described in Fukumoto et al. (1998), Nature Biotech. 16: 267-70. Those of ordinary skill in the art appreciate that each of these references enables one to select different peptides than actually

disclosed therein by following the disclosed procedures with different peptide libraries.

The term "-antagonist peptide" or "inhibitor peptide" refers to a peptide that blocks or in some way interferes with the biological activity of the associated protein of interest, or has biological activity comparable to a known antagonist or inhibitor of the associated protein of interest. Thus, the term "TNF-antagonist peptide" comprises peptides that can be identified or derived as described in Takasaki *et al.* (1997), *Nature Biotech.* 15: 1266-70 or any of the references in Table 2 identified as having TNF-antagonistic subject matter. Those of ordinary skill in the art appreciate that each of these references enables one to select different peptides than actually disclosed therein by following the disclosed procedures with different peptide libraries.

The terms "IL-1 antagonist" and "IL-1ra-mimetic peptide" comprises peptides that inhibit or down-regulate activation of the IL-1 receptor by IL-1. IL-1 receptor activation results from formation of a complex among IL-1, IL-1 receptor, and IL-1 receptor accessory protein. IL-1 antagonist or IL-1ra-mimetic peptides bind to IL-1, IL-1 receptor, or IL-1 receptor accessory protein and obstruct complex formation among any two or three components of the complex. Exemplary IL-1 antagonist or IL-1ra-mimetic peptides can be identified or derived as described in U.S. Pat. Nos. 5,608,035, 5,786,331, 5,880,096, or any of the references in Table 2 identified as having IL-1ra-mimetic or IL-1 antagonistic subject matter. Those of ordinary skill in the art appreciate that each of these references enables one to select different peptides than actually disclosed therein by following the disclosed procedures with different peptide libraries.

The term "VEGF-antagonist peptide" comprises peptides that can be identified or derived as described in Fairbrother (1998), *Biochem.* 37:

17754-64, and in any of the references in Table 2 identified as having VEGF-antagonistic subject matter. Those of ordinary skill in the art appreciate that each of these references enables one to select different peptides than actually disclosed therein by following the disclosed
 5 procedures with different peptide libraries.

The term "MMP inhibitor peptide" comprises peptides that can be identified or derived as described in Koivunen (1999), Nature Biotech. 17: 768-74 and in any of the references in Table 2 identified as having MMP inhibitory subject matter. Those of ordinary skill in the art appreciate that
 10 each of these references enables one to select different peptides than actually disclosed therein by following the disclosed procedures with different peptide libraries.

Additionally, physiologically acceptable salts of the compounds of this invention are also encompassed herein. By "physiologically
 15 acceptable salts" is meant any salts that are known or later discovered to be pharmaceutically acceptable. Some specific examples are: acetate; trifluoroacetate; hydrohalides, such as hydrochloride and hydrobromide; sulfate; citrate; tartrate; glycolate; and oxalate.

Structure of compounds

20 In General. In the compositions of matter prepared in accordance with this invention, the peptide may be attached to the vehicle through the peptide's N-terminus or C-terminus. Thus, the vehicle-peptide molecules of this invention may be described by the following formula I:

I

25
$$(X^1)_a-F^1-(X^2)_b$$

wherein:

F¹ is a vehicle (preferably an Fc domain);

X¹ and X² are each independently selected from -(L¹)_c-P¹, -(L¹)_c-P¹-
 (L²)_d-P², -(L¹)_c-P¹-(L²)_d-P²-(L³)_e-P³, and -(L¹)_c-P¹-(L²)_d-P²-(L³)_e-P³-(L⁴)_f-P⁴

23

P^1 , P^2 , P^3 , and P^4 are each independently sequences of pharmacologically active peptides;

L^1 , L^2 , L^3 , and L^4 are each independently linkers; and

a, b, c, d, e, and f are each independently 0 or 1, provided that at least one of a and b is 1.

Thus, compound I comprises preferred compounds of the formulae

II



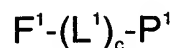
and multimers thereof wherein F^1 is an Fc domain and is attached at the C-terminus of X^1 ;

III



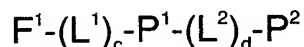
and multimers thereof wherein F^1 is an Fc domain and is attached at the N-terminus of X^2 ;

IV



and multimers thereof wherein F^1 is an Fc domain and is attached at the N-terminus of $-(L^1)_c-P^1$; and

V



and multimers thereof wherein F^1 is an Fc domain and is attached at the N-terminus of $-L^1-P^1-L^2-P^2$.

Peptides. Any number of peptides may be used in conjunction with the present invention. Of particular interest are peptides that mimic the activity of EPO, TPO, growth hormone, G-CSF, GM-CSF, IL-1ra, leptin, CTLA4, TRAIL, TGF- α , and TGF- β . Peptide antagonists are also of interest, particularly those antagonistic to the activity of TNF, leptin, any of the interleukins (IL-1, 2, 3, ...), and proteins involved in complement activation (e.g., C3b). Targeting peptides are also of interest, including

tumor-homing peptides, membrane-transporting peptides, and the like. All of these classes of peptides may be discovered by methods described in the references cited in this specification and other references.

5 Phage display, in particular, is useful in generating peptides for use in the present invention. It has been stated that affinity selection from libraries of random peptides can be used to identify peptide ligands for any site of any gene product. Dedman *et al.* (1993), J. Biol. Chem. 268: 23025-30. Phage display is particularly well suited for identifying peptides that bind to such proteins of interest as cell surface receptors or any
10 proteins having linear epitopes. Wilson *et al.* (1998), Can. J. Microbiol. 44: 313-29; Kay *et al.* (1998), Drug Disc. Today 3: 370-8. Such proteins are extensively reviewed in Herz *et al.* (1997), J. Receptor & Signal Transduction Res. 17(5): 671-776, which is hereby incorporated by reference. Such proteins of interest are preferred for use in this invention.

15 A particularly preferred group of peptides are those that bind to cytokine receptors. Cytokines have recently been classified according to their receptor code. See Inglot (1997), Archivum Immunologiae et Therapiae Experimentalis 45: 353-7, which is hereby incorporated by reference. Among these receptors, most preferred are the CKRs (family I in
20 Table 3). The receptor classification appears in Table 3.

Table 3—Cytokine Receptors Classified by Receptor Code

| Cytokines (ligands) | | Receptor Type | |
|----------------------------|--|---------------------------|---|
| family | subfamily | family | subfamily |
| I. Hematopoietic cytokines | 1. IL-2, IL-4, IL-7, IL-9, IL-13, IL-15 2. IL-3, IL-5, GM-CSF 3. IL-6, IL-11, IL-12, LIF, OSM, CNTF, leptin (OB) 4. G-CSF, EPO, TPO, PRL, GH 5. IL-17, HVS-IL-17 | I. Cytokine R (CKR) | 1. shared γ Cr 2. shared GP 140 β R 3. 3.shared RP 130 4. "single chain" R 5. other R ^c |
| II. IL-10 ligands | IL-10, BCRF-1, HSV-IL-10 | II. IL-10 R | |
| III. Interferons | 1. IFN- α l, α 2, α 4, m, t, IFN- β ^d 2. IFN- γ | III. Interferon R | 1. IFNAR 2. IFNGR |
| IV. IL-1 ligands | 1. IL-1 α , IL-1 β , IL-1Ra | IV. IL-1R | |
| V. TNF ligands | 1. TNF- α , TNF- β (LT), FAS1, CD40 L, CD30L, CD27 L | V. NGF/TNF R ^e | |
| VI. Chemokines | 1. α chemokines: IL-8, GRO α , β , γ , IF-10, PF-4, SDF-1 2. β chemokines: MIP1 α , MIP1 β , MCP-1,2,3,4, RANTES, eotaxin 3. γ chemokines: lymphotactin | VI. Chemokine R | 1. CXCR 2. CCR 3. CR 4. DARC ^f |

^c IL-17R belongs to the CKR family but is not assigned to any of the 4 indicated subfamilies.

^d Other IFN type I subtypes remain unassigned. Hematopoietic cytokines, IL-10 ligands and interferons do not possess functional intrinsic protein kinases. The signaling molecules for the cytokines are JAK's, STATs and related non-receptor molecules. IL-14, IL-16 and IL-18 have been cloned but according to the receptor code they remain unassigned.

^e TNF receptors use multiple, distinct intracellular molecules for signal transduction including "death domain" of FAS R and 55 kDa TNF- α R that participates in their cytotoxic effects. NGF/TNF R can bind both NGF and related factors as well as TNF ligands. Chemokine receptors are G protein-coupled, seven transmembrane (7TM, serpentine) domain receptors.

^f The Duffy blood group antigen (DARC) is an erythrocyte receptor that can bind several different chemokines. It belongs to the immunoglobulin superfamily but characteristics of its signal transduction events remain unclear.

| | | | |
|---------------------|--|----------|--|
| VII. Growth factors | 1.1 SCF, M-CSF, PDGF-AA, AB, BB, FLT-3L, VEGF, SSV- PDGF 1.2 FGF α , FGF β 1.3 EGF, TGF- α , VV-F19 (EGF- like) 1.4 IGF-I, IGF-II, Insulin 1.5 NGF, BDNF, NT-3, NT-4 ^g 2. TGF- β 1, β 2, β 3 | VII. RKF | 1. TK sub-family 1.1 IgTK III R 1.2 IgTK IV R 1.3 Cysteine-rich TK-I 1.4 Cysteine rich TK-II 1.5 Cysteine knot TK V 2. STK subfamily ^h |
|---------------------|--|----------|--|

Exemplary peptides for this invention appear in Tables 4 through 20 below. These peptides may be prepared by methods disclosed in the art. Single letter amino acid abbreviations are used. The X in these sequences (and throughout this specification, unless specified otherwise in a particular instance) means that any of the 20 naturally occurring amino acid residues may be present. Any of these peptides may be linked in tandem (i.e., sequentially), with or without linkers, and a few tandem-linked examples are provided in the table. Linkers are listed as "Λ" and may be any of the linkers described herein. Tandem repeats and linkers are shown separated by dashes for clarity. Any peptide containing a cysteinyl residue may be cross-linked with another Cys-containing peptide, either or both of which may be linked to a vehicle. A few cross-linked examples are provided in the table. Any peptide having more than one Cys residue may form an intrapeptide disulfide bond, as well; see, for example, EPO-mimetic peptides in Table 5. A few examples of intrapeptide disulfide-bonded peptides are specified in the table. Any of these peptides may be derivatized as described herein, and a few derivatized examples are provided in the table. Derivatized peptides in

^g The neurotrophic cytokines can associate with NGF/TNF receptors also.

the tables are exemplary rather than limiting, as the associated underivatized peptides may be employed in this invention, as well. For derivatives in which the carboxyl terminus may be capped with an amino group, the capping amino group is shown as $-NH_2$. For derivatives in

5 which amino acid residues are substituted by moieties other than amino acid residues, the substitutions are denoted by σ , which signifies any of the moieties described in Bhatnagar *et al.* (1996), *J. Med. Chem.* 39: 3814-9 and Cuthbertson *et al.* (1997), *J. Med. Chem.* 40: 2876-82, which are incorporated by reference. The J substituent and the Z substituents (Z_5 , Z_6 ,

10 $\dots Z_{40}$) are as defined in U.S. Pat. Nos. 5,608,035, 5,786,331, and 5,880,096, which are incorporated by reference. For the EPO-mimetic sequences (Table 5), the substituents X_2 through X_{11} and the integer "n" are as defined in WO 96/40772, which is incorporated by reference. The substituents " Ψ ," " Θ ," and "+" are as defined in Sparks *et al.* (1996), *Proc. Natl. Acad. Sci.* 93:

15 1540-4, which is hereby incorporated by reference. X_4 , X_5 , X_6 , and X_7 are as defined in U.S. Pat. No. 5,773,569, which is hereby incorporated by reference, except that: for integrin-binding peptides, X_1 , X_2 , X_3 , X_4 , X_5 , X_6 , X_7 , and X_8 are as defined in International applications WO 95/14714, published June 1, 1995 and WO 97/08203, published March 6, 1997, which

20 are also incorporated by reference; and for VIP-mimetic peptides, X_1 , X_1' , X_1'' , X_2 , X_3 , X_4 , X_5 , X_6 and Z and the integers m and n are as defined in WO 97/40070, published October 30, 1997, which is also incorporated by reference. Xaa and Yaa below are as defined in WO 98/09985, published March 12, 1998, which is incorporated by reference. AA_1 , AA_2 , AB_1 , AB_2 ,

25 and AC are as defined in International application WO 98/53842, published December 3, 1998, which is incorporated by reference. X^1 , X^2 , X^3 , and X^4 in Table 17 only are as defined in European application EP 0 911

ⁿ STKS may encompass many other TGF- β -related factors that remain unassigned. The protein kinases are intrinsic part of the intracellular domain of receptor kinase family (RKF). The enzymes participate in the signals transmission via the receptors.

393, published April 28, 1999. Residues appearing in boldface are D-amino acids. All peptides are linked through peptide bonds unless otherwise noted. Abbreviations are listed at the end of this specification. In the "SEQ ID NO." column, "NR" means that no sequence listing is required for the given sequence.

Table 4—IL-1 antagonist peptide sequences

| Sequence/structure | SEQ ID NO: |
|--|------------|
| <u>Z₁₁</u> <u>Z₇</u> <u>Z₈</u> <u>QZ₅</u> <u>YZ₆</u> <u>Z₉</u> <u>Z₁₀</u> | 212 |
| XXQZ ₅ YZ ₆ XX | 907 |
| Z ₇ XQZ ₅ YZ ₆ XX | 908 |
| <u>Z₇</u> <u>Z₈</u> <u>QZ₅</u> <u>YZ₆</u> <u>Z₉</u> <u>Z₁₀</u> | 909 |
| <u>Z₁₁</u> <u>Z₇</u> <u>Z₈</u> <u>QZ₅</u> <u>YZ₆</u> <u>Z₉</u> <u>Z₁₀</u> | 910 |
| <u>Z₁₂</u> <u>Z₁₃</u> <u>Z₁₄</u> <u>Z₁₅</u> <u>Z₁₆</u> <u>Z₁₇</u> <u>Z₁₈</u> <u>Z₁₉</u> <u>Z₂₀</u> <u>Z₂₁</u> <u>Z₂₂</u> <u>Z₁₁</u> <u>Z₇</u> <u>Z₈</u> <u>QZ₅</u> <u>YZ₆</u> <u>Z₉</u> <u>Z₁₀</u> L | 917 |
| <u>Z₂₃</u> <u>NZ₂₄</u> <u>Z₂₅</u> <u>Z₂₆</u> <u>Z₂₇</u> <u>Z₂₈</u> <u>Z₂₉</u> <u>Z₃₀</u> <u>Z₄₀</u> | 979 |
| TANVSSFEWTPYYWQPYALPL | 213 |
| SWTDYGYWQPYALPISGL | 214 |
| ETPFTWEESNAYYWQPYALPL | 215 |
| ENTYSPNWADSMYWQPYALPL | 216 |
| SVGEDHNFWTSEYWQPYALPL | 217 |
| DGYDRWRQSGERYWQPYALPL | 218 |
| FEWTPGYWQPY | 219 |
| FEWTPGYWQHY | 220 |
| FEWTPGWYQJY | 221 |
| AcFEWTPGWYQJY | 222 |
| FEWTPGWpYQJY | 223 |
| FAWTPGYWQJY | 224 |
| FEWAPGYWQJY | 225 |
| FEWVPGYWQJY | 226 |
| FEWTPGYWQJY | 227 |
| AcFEWTPGYWQJY | 228 |
| FEWTPaWYQJY | 229 |
| FEWTPSarWYQJY | 230 |
| FEWTPGYYQPY | 231 |
| FEWTPGWWQPY | 232 |
| FEWTPNYWQPY | 233 |
| FEWTPvYWQJY | 234 |
| FEWTPecGYWQJY | 235 |
| FEWTPAibYWQJY | 236 |
| FEWTSarGYWQJY | 237 |
| FEWTPGYWQPY | 238 |
| FEWTPGYWQHY | 239 |
| FEWTPGWYQJY | 240 |

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|-----------------|-----|
| AcFEWTPGWYQJY | 241 |
| FEWTPGW-pY-QJY | 242 |
| FAWTPGYWQJY | 243 |
| FEWAPGYWQJY | 244 |
| FEWVPGYWQJY | 245 |
| FEWTPGYWQJY | 246 |
| AcFEWTPGYWQJY | 247 |
| FEWTPAWYQJY | 248 |
| FEWTPSarWYQJY | 249 |
| FEWTPGYYQPY | 250 |
| FEWTPGWWQPY | 251 |
| FEWTPNYWQPY | 252 |
| FEWTPVYWQJY | 253 |
| FEWTPecGYWQJY | 254 |
| FEWTPAibYWQJY | 255 |
| FEWTSarGYWQJY | 256 |
| FEWTPGYWQPYALPL | 257 |
| 1NapEWTPGYYQJY | 258 |
| YEWTPGYYQJY | 259 |
| FEWVPGYYQJY | 260 |
| FEWTPSYQJY | 261 |
| FEWTPNYYQJY | 262 |
| TKPR | 263 |
| RKSSK | 264 |
| RKQDK | 265 |
| NRKQDK | 266 |
| RKQDKR | 267 |
| ENRKQDKRF | 268 |
| VTKFYF | 269 |
| VTKFY | 270 |
| VTDFY | 271 |
| SHLYWQPYSVQ | 671 |
| TLVYWQPYSLQT | 672 |
| RGDYWQPYSVQS | 673 |
| VHVVWQPYSVQT | 674 |
| RLVYWQPYSVQT | 675 |
| SRVWFQPYSLQS | 676 |
| NMVYWQPYSIQT | 677 |
| SVVFWQPYSVQT | 678 |
| TFVYWQPYALPL | 679 |
| TLVYWQPYSIQR | 680 |
| RLVYWQPYSVQR | 681 |
| SPVFWQPYSIQI | 682 |
| WIEWWQPYSVQS | 683 |
| SLIYWQPYSLQM | 684 |
| TRLYWQPYSVQR | 685 |
| RCDYWQPYSVQT | 686 |
| MRVFWQPYSVQN | 687 |
| KIVYWQPYSVQT | 688 |
| RHLYWQPYSVQR | 689 |

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|---------------|-----|
| ALVWWQPYSEI | 690 |
| SRVWFQPYSLQS | 691 |
| WEQPYALPLE | 692 |
| QLVWWQPYSVQR | 693 |
| DLRYWQPYSVQV | 694 |
| ELVWWQPYSLQL | 695 |
| DLVWWQPYSVQW | 696 |
| NGNYWQPYSFQV | 697 |
| ELVYWQPYSIQR | 698 |
| ELMYWQPYSVQE | 699 |
| NLLYWQPYSMQD | 700 |
| GYEWYQPYSVQR | 701 |
| SRVWYQPYSVQR | 702 |
| LSEQYQPYSVQR | 703 |
| GGGWWQPYSVQR | 704 |
| VGRWYQPYSVQR | 705 |
| VHVYWQPYSVQR | 706 |
| QARWYQPYSVQR | 707 |
| VHVYWQPYSVQT | 708 |
| RSVYWQPYSVQR | 709 |
| TRVWFQPYSVQR | 710 |
| GRIWFQPYSVQR | 711 |
| GRVWFQPYSVQR | 712 |
| ARTWYQPYSVQR | 713 |
| ARVWWQPYSVQM | 714 |
| RLMFYQPYSVQR | 715 |
| ESMWYQPYSVQR | 716 |
| HFGWWQPYSVHM | 717 |
| ARFWWQPYSVQR | 718 |
| RLVYWQ PYAPIY | 719 |
| RLVYWQ PYSYQT | 720 |
| RLVYWQ PYSLPI | 721 |
| RLVYWQ PYSVQA | 722 |
| SRVWYQ PYAKGL | 723 |
| SRVWYQ PYAQGL | 724 |
| SRVWYQ PYAMPL | 725 |
| SRVWYQ PYSVQA | 726 |
| SRVWYQ PYSLGL | 727 |
| SRVWYQ PYAREL | 728 |
| SRVWYQ PYSRQP | 729 |
| SRVWYQ PYFVQP | 730 |
| EYEWYQ PYALPL | 731 |
| IPEYWQ PYALPL | 732 |
| SRIWWQ PYALPL | 733 |
| DPLFWQ PYALPL | 734 |
| SRQWVQ PYALPL | 735 |
| IRSWWQ PYALPL | 736 |
| RGYWQ PYALPL | 737 |
| RLLWVQ PYALPL | 738 |
| EYRWVQ PYALPL | 739 |

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|-----------------------|-----|
| DAYWVQ PYALPL | 740 |
| WSGYFQ PYALPL | 741 |
| NIEFWQ PYALPL | 742 |
| TRDWVQ PYALPL | 743 |
| DSSWYQ PYALPL | 744 |
| IGNWYQ PYALPL | 745 |
| NLRWDQ PYALPL | 746 |
| LPEFWQ PYALPL | 747 |
| DSYWWQ PYALPL | 748 |
| RSQYYQ PYALPL | 749 |
| ARFWLQ PYALPL | 750 |
| NSYFWQ PYALPL | 751 |
| RFMYWQPYSVQR | 752 |
| AHLFWQPYSVQR | 753 |
| WWQPYALPL | 754 |
| YYQPYALPL | 755 |
| YFQPYALGL | 756 |
| YWYQPYALPL | 757 |
| RWWQPYATPL | 758 |
| GWYQPYALGF | 759 |
| YWYQPYALGL | 760 |
| IWYQPYAMPL | 761 |
| SNMQPYQRLS | 762 |
| TFVYWQPY AVGLPAAETACN | 763 |
| TFVYWQPY SVQMTITGKVTM | 764 |
| TFVYWQPY SSHXXVPXGFPL | 765 |
| TFVYWQPY YGNPQWAIHVRH | 766 |
| TFVYWQPY VLELPEGAVRA | 767 |
| TFVYWQPY VDYVWPIPIAQV | 768 |
| GWYQPYVDGWR | 769 |
| RWEQPYVKDGWS | 770 |
| EWYQPYALGWAR | 771 |
| GWWQPYARGL | 772 |
| LFEQPYAKALGL | 773 |
| GWEQPYARGLAG | 774 |
| AWVQPYATPLDE | 775 |
| MWYQPYSSQPAE | 776 |
| GWTQPYSSQGEV | 777 |
| DWFQPYSIQSDE | 778 |
| PWQPYARGFG | 779 |
| RPLYWQPYSVQV | 780 |
| TLIYWQPYSVQI | 781 |
| RFDYWQPYSDQT | 782 |
| WHQFVQPYALPL | 783 |
| EWDS VYWQPYSVQ TLLR | 784 |
| WEQN VYWQPYSVQ SFAD | 785 |
| SDV VYWQPYSVQ SLEM | 786 |
| YYDG VYWQPYSVQ VMPA | 787 |
| SDIWWQ PYALPL | 788 |
| QRIWWQ PYALPL | 789 |

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| SRIWWQ PYALPL | 790 |
| RSLYWQ PYALPL | 791 |
| TIIWEQ PYALPL | 792 |
| WETWYQ PYALPL | 793 |
| SYDWEQ PYALPL | 794 |
| SRIWCQ PYALPL | 795 |
| EIMFWQ PYALPL | 796 |
| DYVWQQ PYALPL | 797 |
| MDLLVQ WYQPYALPL | 798 |
| GSKVIL WYQPYALPL | 799 |
| RQGANI WYQPYALPL | 800 |
| GGGDEP WYQPYALPL | 801 |
| SQLERT WYQPYALPL | 802 |
| ETWVRE WYQPYALPL | 803 |
| KKGSTQ WYQPYALPL | 804 |
| LQARMN WYQPYALPL | 805 |
| EPRSQK WYQPYALPL | 806 |
| VKQKWR WYQPYALPL | 807 |
| LRRHDV WYQPYALPL | 808 |
| RSTASI WYQPYALPL | 809 |
| ESKEDQ WYQPYALPL | 810 |
| EGLTMK WYQPYALPL | 811 |
| EGSREG WYQPYALPL | 812 |
| VIEWWQ PYALPL | 813 |
| VWYWEQ PYALPL | 814 |
| ASEWWQ PYALPL | 815 |
| FYEWWQ PYALPL | 816 |
| EGWWVQ PYALPL | 817 |
| WGEWLQ PYALPL | 818 |
| DYVWEQ PYALPL | 819 |
| AHTWWQ PYALPL | 820 |
| FIEWFQ PYALPL | 821 |
| WLAWEQ PYALPL | 822 |
| VMEWWQ PYALPL | 823 |
| ERMWQ PYALPL | 824 |
| NXXWXX PYALPL | 825 |
| WGNWYQ PYALPL | 826 |
| TLYWEQ PYALPL | 827 |
| VWRWEQ PYALPL | 828 |
| LLWTQ PYALPL | 829 |
| SRIWXX PYALPL | 830 |
| SDIWYQ PYALPL | 831 |
| WGYYXX PYALPL | 832 |
| TSGWYQ PYALPL | 833 |
| VHPYXX PYALPL | 834 |
| EHSYFQ PYALPL | 835 |
| XXIWYQ PYALPL | 836 |
| AQLHSQ PYALPL | 837 |
| WANWFQ PYALPL | 838 |
| SRLYSQ PYALPL | 839 |

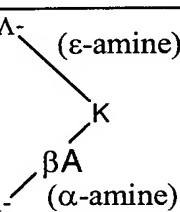
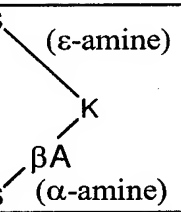
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|-------------------------|-----|
| GVTFSQ PYALPL | 840 |
| SIVWSQ PYALPL | 841 |
| SRDLVQ PYALPL | 842 |
| HWGH VYWQPYSVQ DDLG | 843 |
| SWHS VYWQPYSVQ SVPE | 844 |
| WRDS VYWQPYSVQ PESA | 845 |
| TWDA VYWQPYSVQ KWLD | 846 |
| TPPW VYWQPYSVQ SLDP | 847 |
| YWSS VYWQPYSVQ SVHS | 848 |
| YWY QPY ALGL | 849 |
| YWY QPY ALPL | 850 |
| EWI QPY ATGL | 851 |
| NWE QPY AKPL | 852 |
| AFY QPY ALPL | 853 |
| FLY QPY ALPL | 854 |
| VCK QPY LEWC | 855 |
| ETPFTWEESNAYYWQPYALPL | 856 |
| QGWLTWQDSVDMYWQPYALPL | 857 |
| FSEAGYTPENTYWQPYALPL | 858 |
| TESPGGLDWAKIYWQPYALPL | 859 |
| DGYDRWRQSGERYWQPYALPL | 860 |
| TANVSSFEWTPGYWQPYALPL | 861 |
| SVGEDHNFWTSE YWQPYALPL | 862 |
| MNDQTSEVSTFP YWQPYALPL | 863 |
| SWSEAFEQPRNL YWQPYALPL | 864 |
| QYAEPSALNDWG YWQPYALPL | 865 |
| NGDWATADWSNY YWQPYALPL | 866 |
| THDEHI YWQPYALPL | 867 |
| MLEKTYTTWTPG YWQPYALPL | 868 |
| WSDPLTRDADL YWQPYALPL | 869 |
| SDAFTTQDSQAM YWQPYALPL | 870 |
| GDDAAWRTDSL YWQPYALPL | 871 |
| AIIRQLYRWSEM YWQPYALPL | 872 |
| ENTYSPNWADSM YWQPYALPL | 873 |
| MNDQTSEVSTFP YWQPYALPL | 874 |
| SVGEDHNFWTSE YWQPYALPL | 875 |
| QTPFTWEESNAY YWQPYALPL | 876 |
| ENPFTWQESNAY YWQPYALPL | 877 |
| VTPFTWEDSNVF YWQPYALPL | 878 |
| QIPFTWEQSNAY YWQPYALPL | 879 |
| QAPLWQESAAY YWQPYALPL | 880 |
| EPTFTWEESKAT YWQPYALPL | 881 |
| TTTTLWEEESNAY YWQPYALPL | 882 |
| ESPLTWEESSAL YWQPYALPL | 883 |
| ETPLTWEEESNAY YWQPYALPL | 884 |
| EATFTWAESNAY YWQPYALPL | 885 |
| EALFTWKESTAY YWQPYALPL | 886 |
| STP-TWEESNAY YWQPYALPL | 887 |
| ETPFTWEESNAY YWQPYALPL | 888 |
| KAPFTWEESQAY YWQPYALPL | 889 |

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|------------------------|-----|
| STSFTWEESNAY YWQPYALPL | 890 |
| DSTFTWEESNAY YWQPYALPL | 891 |
| YIPFTWEESNAY YWQPYALPL | 892 |
| QTAFTWEESNAY YWQPYALPL | 893 |
| ETLFTWEESNAT YWQPYALPL | 894 |
| VSSFTWEESNAY YWQPYALPL | 895 |
| QPYALPL | 896 |
| Py-1-NapPYQJYALPL | 897 |
| TANVSSFEWTPG YWQPYALPL | 898 |
| FEWTPGYWQPYALPL | 899 |
| FEWTPGYWQJYALPL | 900 |
| FEWTPGYYQJYALPL | 901 |
| ETPFTWEESNAYYWQPYALPL | 902 |
| FTWEESNAYYWQJYALPL | 903 |
| ADVL YWQPYA PVTLWV | 904 |
| GDVAE YWQPYA LPLTSL | 905 |
| SWTDYG YWQPYA LPISGL | 906 |
| FEWTPGYWQPYALPL | 911 |
| FEWTPGYWQJYALPL | 912 |
| FEWTPGWWQPYALPL | 913 |
| FEWTPGWWQJYALPL | 914 |
| FEWTPGYYQPYALPL | 915 |
| FEWTPGYYQJYALPL | 916 |
| TANVSSFEWTPGYWQPYALPL | 918 |
| SWTDYGYWQPYALPISGL | 919 |
| ETPFTWEESNAYYWQPYALPL | 920 |
| ENTYSPNWADSMYWQPYALPL | 921 |
| SVGEDHNFWTSEYWQPYALPL | 922 |
| DGYDRWRQSGERYWQPYALPL | 923 |
| FEWTPGYWQPYALPL | 924 |
| FEWTPGYWQPY | 925 |
| FEWTPGYWQJY | 926 |
| EWTPGYWQPY | 927 |
| FEWTPGWWQJY | 928 |
| AEWTPGYWQJY | 929 |
| FAWTPGYWQJY | 930 |
| FEATPGYWQJY | 931 |
| FEWAPGYWQJY | 932 |
| FEWTAGYWQJY | 933 |
| FEWTPAYWQJY | 934 |
| FEWTPGAWQJY | 935 |
| FEWTPGYAQJY | 936 |
| FEWTPGYWQJA | 937 |
| FEWTTGGYWQJY | 938 |
| FEWTPGYWQJY | 939 |
| FEWTJGYWQJY | 940 |
| FEWTPecGYWQJY | 941 |
| FEWTPAibYWQJY | 942 |
| FEWTPSarWYQJY | 943 |
| FEWTSarGYWQJY | 944 |

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| FEWTPNYWQJY | 945 |
| FEWTPVYWQJY | 946 |
| FEWTPPYWQJY | 947 |
| AcFEWTPGWYQJY | 948 |
| AcFEWTPGYWQJY | 949 |
| INap-EWTPGYYQJY | 950 |
| YEWTPGYYQJY | 951 |
| FEWVPGYYQJY | 952 |
| FEWTPGYYQJY | 953 |
| FEWTPsYYQJY | 954 |
| FEWTPnYYQJY | 955 |
| SHLY-Nap-QPYSVQM | 956 |
| TLVY-Nap-QPYSLQT | 957 |
| RGDY-Nap-QPYSVQS | 958 |
| NMVY-Nap-QPYSIQT | 959 |
| VYWQPYSVQ | 960 |
| VY-Nap-QPYSVQ | 961 |
| TFVYWQJYALPL | 962 |
| FEWTPGYYQJ-Bpa | 963 |
| XaaFEWTPGYYQJ-Bpa | 964 |
| FEWTPGY-Bpa-QJY | 965 |
| AcFEWTPGY-Bpa-QJY | 966 |
| FEWTPG-Bpa-YQJY | 967 |
| AcFEWTPG-Bpa-YQJY | 968 |
| AcFE-Bpa-TPGYYQJY | 969 |
| AcFE-Bpa-TPGYYQJY | 970 |
| Bpa-EWTPGYYQJY | 971 |
| AcBpa-EWTPGYYQJY | 972 |
| VYWQPYSVQ | 973 |
| RLVYWQPYSVQR | 974 |
| RLVY-Nap-QPYSVQR | 975 |
| RLDYWQPYSVQR | 976 |
| RLVWFQPYSVQR | 977 |
| RLVYWQPYSIQR | 978 |
| DNSSWYDSFLL | 980 |
| DNTAWYESFLA | 981 |
| DNTAWYENFLL | 982 |
| PARE DNTAWYDSFLI WC | 983 |
| TSEY DNTTWYKFLA SQ | 984 |
| SQIP DNTAWYQSFLH HG | 985 |
| SPFI DNTAWYENFLL TY | 986 |
| EQIY DNTAWYDHFL SY | 987 |
| TPFI DNTAWYENFLL TY | 988 |
| TYTY DNTAWYERFLM SY | 989 |
| TMTQ DNTAWYENFLL SY | 990 |
| TI DNTAWYANLVQ TYPQ | 991 |
| TI DNTAWYERFLA QYPD | 992 |
| HI DNTAWYENFLL TYTP | 993 |
| SQ DNTAWYENFLL SYKA | 994 |
| QI DNTAWYERFL QYNA | 995 |

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|-----------------------|------|
| NQ DNTAWYESFLL QYNT | 996 |
| TI DNTAWYENFLL NHNL | 997 |
| HY DNTAWYERFLQ QGWH | 998 |
| ETPFTWEESNAYYWQPYALPL | 999 |
| YIPFTWEESNAYYWQPYALPL | 1000 |
| DGYDRWRQSGERYWQPYALPL | 1001 |
| pY-INap-pY-QJYALPL | 1002 |
| TANVSSFEWTPGYWQPYALPL | 1003 |
| FEWTPGYWQJYALPL | 1004 |
| FEWTPGYWQPYALPLSD | 1005 |
| FEWTPGYYQJYALPL | 1006 |
| FEWTPGYWQJY | 1007 |
| AcFEWTPGYWQJY | 1008 |
| AcFEWTPGWYQJY | 1009 |
| AcFEWTPGYYQJY | 1010 |
| AcFEWTPaYWQJY | 1011 |
| AcFEWTPaWYQJY | 1012 |
| AcFEWTPaYYQJY | 1013 |
| FEWTPGYYQJYALPL | 1014 |
| FEWTPGYWQJYALPL | 1015 |
| FEWTPGWYQJYALPL | 1016 |
| TANVSSFEWTPGYWQPYALPL | 1017 |
| AcFEWTPGYWQJY | 1018 |
| AcFEWTPGWYQJY | 1019 |
| AcFEWTPGYYQJY | 1020 |
| AcFEWTPAYWQJY | 1021 |
| AcFEWTPAWYQJY | 1022 |
| AcFEWTPAYYQJY | 1023 |

Table 5—EPO-mimetic peptide sequences

| Sequence/structure | SEQ ID NO: |
|--|------------|
| YXCXXGPXTWXCXP | 83 |
| YXCXXGPXTWXCXP-YXCXXGPXTWXCXP | 84 |
| YXCXXGPXTWXCXP- Λ -YXCXXGPXTWXCXP | 85 |
| YXCXXGPXTWXCXP- Λ -  (ε-amine) K βA (α-amine) YXCXXGPXTWXCXP- Λ - | 86 |
| GGTYSCHFGPLTWVCKPQGG | 87 |
| GGDYHCRMGPLTWVCKPLGG | 88 |
| GGVYACRMGPITWVCSPLGG | 89 |
| VGNYMCHFGPITWVCRPGGG | 90 |
| GGLYLGRFGPVTWDCGYKGG | 91 |
| GGTYSCHFGPLTWVCKPQGG- GGTYSCHFGPLTWVCKPQGG | 92 |
| GGTYSCHFGPLTWVCKPQGG- Λ - GGTYSCHFGPLTWVCKPQGG | 93 |
| GGTYSCHFGPLTWVCKPQGGSSK | 94 |
| GGTYSCHFGPLTWVCKPQGGSSK- GGTYSCHFGPLTWVCKPQGGSSK | 95 |
| GGTYSCHFGPLTWVCKPQGGSSK- Λ - GGTYSCHFGPLTWVCKPQGGSSK | 96 |
| GGTYSCHFGPLTWVCKPQGGSS  (ε-amine) K βA (α-amine) | 97 |
| GGTYSCHFGPLTWVCKPQGGSS- GGTYSCHFGPLTWVCKPQGGSS | 97 |
| GGTYSCHFGPLTWVCKPQGGSSK(- Λ -biotin) | 98 |
| CX ₄ X ₅ GPX ₆ TWX ₇ C | 421 |
| GGTYSCHGPLTWVCKPQGG | 422 |
| VGNVMAHMGPIWVCRPGG | 423 |
| GGPHHVYACRMGPLTWIC | 424 |
| GGTYSCHFGPLTWVCKPQ | 425 |
| GGLYACHMGPMTWVCQPLRG | 426 |
| TIAQYICYMGPEWECRPSKA | 427 |
| YSCHFGPLTWVCK | 428 |
| YCHFGPLTWVC | 429 |
| X ₂ X ₃ X ₄ GPX ₅ TWX ₆ X ₇ | 124 |
| YX ₂ X ₃ X ₄ X ₅ GPX ₆ TWX ₇ X ₈ | 461 |

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|---|------|
| X ₁ YX ₂ X ₃ X ₄ X ₅ GPX ₆ TWX ₇ X ₈ X ₉ X ₁₀ X ₁₁ | 419 |
| X ₁ YX ₂ CX ₃ X ₄ GPX ₅ TWX ₆ CX ₇ X ₈ X ₉ X ₁₀ X ₁₁ | 420 |
| GGLYLCRFGPVTWDCGYKGG | 1024 |
| GGTYSCHFGPLTWVCKPQGG | 1025 |
| GGDYHCRMGPPLTWVCKPLGG | 1026 |
| VGNYMCHFGPITWVCRPGGG | 1029 |
| GGVYACRMGPITWVCSPLGG | 1030 |
| VGNYMAHMGPIWVCRPGG | 1035 |
| GGTYSCHFGPLTWVCKPQ | 1036 |
| GGLYACHMGPMWVQCPLRG | 1037 |
| TIAQYICYMGPETWECRPSKA | 1038 |
| YSCHFGPLTWVCK | 1039 |
| YCHFGPLTWVC | 1040 |
| SCHFGPLTWVCK | 1041 |
| (AX ₂)X ₃ X ₄ X ₅ GPX ₆ TWX ₇ X ₈ | 1042 |

Table 6—TPO-mimetic peptide sequences

| Sequence/structure | SEQ ID NO: |
|---|------------|
| IEGPTLRQWLAARA | 13 |
| IEGPTLRQWLAACA | 24 |
| IEGPTLRWLAARA | 25 |
| IEGPTLRQWLAARA- Δ -IEGPTLRQWLAARA | 26 |
| IEGPTLRQWLAACA- Δ -IEGPTLRQWLAACA | 27 |
| IEGPTLRQCLAARA- Δ -IEGPTLRQCLAARA ----- | 28 |
| IEGPTLRQWLAARA- Δ -K(BrAc)- Δ -IEGPTLRQWLAARA | 29 |
| IEGPTLRQWLAARA- Δ -K(PEG)- Δ -IEGPTLRQWLAARA | 30 |
| IEGPTLRQCLAARA- Δ -IEGPTLRQWLAARA | 31 |
| IEGPTLRQCLAARA- Δ -IEGPTLRQWLAARA | 31 |
| IEGPTLRQWLAARA- Δ -IEGPTLRQCLAARA | 32 |
| IEGPTLRQWLAARA- Δ -IEGPTLRQCLAARA | 32 |
| VRDQIXXXL | 33 |
| TLREWL | 34 |
| GRVRDQVAGW | 35 |
| GRVKDQIAQL | 36 |
| GVRDQVSWAL | 37 |
| ESVREQVMKY | 38 |
| SVRSQISASL | 39 |
| GVRETVYRHM | 40 |
| GVREVIVMHML | 41 |
| GRVRDQIWAAL | 42 |
| AGVRDQILIWL | 43 |
| GRVRDQIMLSL | 44 |
| GRVRDQI(X) ₂ L | 45 |
| CTLRQWLQGC | 46 |
| CTLQEFLEG | 47 |
| CTRTEWLHGC | 48 |
| CTLREWLHGGFC | 49 |
| CTLREWVFAGLC | 50 |
| CTLRQWLILLGMC | 51 |
| CTLAEFLLASGVEQC | 52 |
| CSLQEFLLSHGGYVC | 53 |
| CTLREFLDPTTAVC | 54 |
| CTLKEWLVSHEVWC | 55 |
| CTLREWL(X) _{2,6} C | 56-60 |
| REGPTLRQWM | 61 |
| EGPTLRQWLA | 62 |
| ERGPFWAKAC | 63 |
| REGPRCVMWM | 64 |
| CGTEGPTLSTWLDG | 65 |

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|--------------------------------------|-------|
| CEQDGPTLLEWLKC | 66 |
| CELVGPSLMSWLTC | 67 |
| CLTGPFVTQWLYEC | 68 |
| CRAGPTLLEWLTLC | 69 |
| CADGPTLREWISFC | 70 |
| $C(X)_{1,2}$ EGPTLREWL $(X)_{1,2}$ C | 71-74 |
| GGCTLREWLHGGFCGG | 75 |
| GGCADGPTLREWISFCGG | 76 |
| GNADGPTLRQWLEGRRPKN | 77 |
| LAIEGPTLRQWLHGNGRDT | 78 |
| HGRVGPTLREWKTQVATKK | 79 |
| TIKGPTLRQWLKSREHTS | 80 |
| ISDGPTLKEWLSVTRGAS | 81 |
| SIEGPTLREWLTSRTPHS | 82 |

Table 7—G-CSF-mimetic peptide sequences

| Sequence/structure | SEQ ID NO: |
|-------------------------|---------------|
| EEDCK | 99 |
| EEDCK | 99 |
| EEDCK | 99 |
| EED σ K | 100 |
| EED σ K | 100 |
| EED σ K | 100 |
| pGluED σ K | 101 |
| pGluED σ K | 101 |
| pGluED σ K | 101 |
| PicSD σ K | 102 |
| PicSD σ K | 102 |
| PicSD σ K | 102 |
| EEDCK- Λ -EEDCK | 103 |
| EEDXK- Λ -EEDXK | 104 |

Table 8—TNF-antagonist peptide sequences

| Sequence/structure | SEQ ID NO: |
|--|------------|
| YCFTASENHCY | 106 |
| YCFTNSENHCY | 107 |
| YCFTRSENHCY | 108 |
| FCASENHCY | 109 |
| YCASENHCY | 110 |
| FCNSENHCY | 111 |
| FCNSENRCY | 112 |
| FCNSVENRCY | 113 |
| YCSQSVSND CF | 114 |
| FCVSNDRCY | 115 |
| YCRKELGQVCY | 116 |
| YCKEPGQCY | 117 |
| YCRKEMGCV | 118 |
| FCRKEMGCV | 119 |
| YCWSQNLCY | 120 |
| YCELSQYLCY | 121 |
| YCWSQNYCY | 122 |
| YCWSQYLCY | 123 |
| DFLPHYKNTSLGHRP | 1085 |
| $ \begin{array}{c} AA_1-AB_1 \\ \quad \quad \backslash \\ \quad \quad \quad AC \\ \quad \quad / \\ AA_2-AB_2 \end{array} $ | NR |

Table 9—Integrin-binding peptide sequences

| Sequence/structure | SEQ ID NO: |
|---|------------|
| RX ₁ ETX ₂ WX ₃ | 441 |
| RX ₁ ETX ₂ WX ₃ | 442 |
| RGDGX | 443 |
| CRGDGXC | 444 |
| CX ₁ X ₂ RLDX ₃ X ₄ C | 445 |
| CARRLDAPC | 446 |
| CPSRLDSPC | 447 |
| X ₁ X ₂ X ₃ RGDX ₄ X ₅ X ₆ | 448 |
| CX ₂ CRGDCX ₅ C | 449 |
| CDCRGDCFC | 450 |
| CDCRGDCLC | 451 |
| CLCRGDCIC | 452 |
| X ₁ X ₂ DDX ₃ X ₄ X ₅ X ₆ | 453 |
| X ₁ X ₂ X ₃ DDX ₄ X ₅ X ₆ X ₇ X ₈ | 454 |
| CWDDGWLC | 455 |
| CWDDLWWLC | 456 |
| CWDDGLMC | 457 |
| CWDDGWMC | 458 |
| CSWDDGWLC | 459 |
| CPDDLWWLC | 460 |
| NGR | NR |
| GSL | NR |
| RGD | NR |
| CGRECPRLCQSSC | 1071 |
| CNGRCVSGCAGRC | 1072 |
| CLSGSLSC | 1073 |
| RGD | NR |
| NGR | NR |
| GSL | NR |
| NGRAHA | 1074 |
| CNGRC | 1075 |
| CDCRGDCFC | 1076 |
| CGSLVRC | 1077 |
| DLXXL | 1043 |
| RTDLDSLRTYTL | 1044 |
| RTDLDSLRTY | 1053 |
| RTDLDSLRT | 1054 |
| RTDLDSLRL | 1078 |
| GDLDLLKLRLTL | 1079 |
| GDLHSLRQLLSR | 1080 |
| RDDLHMLRLQLW | 1081 |
| SSDLHALKKRYG | 1082 |
| RGDLKQLSELTW | 1083 |
| RGDLAALSAPPV | 1084 |

Table 10—Selectin antagonist peptide sequences

| Sequence/structure | SEQ ID NO: |
|---------------------|------------|
| DITWDQLWDLMK | 147 |
| DITWDELWKIMN | 148 |
| DYTWFEWLWDMMQ | 149 |
| QITWAQLWNMMK | 150 |
| DMTWHDLWTLMS | 151 |
| DYSWHDLWEVMS | 152 |
| EITWDQLWEVMN | 153 |
| HVSWEQLWDIMN | 154 |
| HITWDQLWRIMT | 155 |
| RNMSWLELWEHMK | 156 |
| AEWTWDQLWHVMNPAESQ | 157 |
| HRAEWLALWEQMSP | 158 |
| KKEDWLALWRIMSV | 159 |
| ITWDQLWDLMK | 160 |
| DITWDQLWDLMK | 161 |
| DITWDQLWDLMK | 162 |
| DITWDQLWDLMK | 163 |
| CQNRYTDLVAIQNKNE | 462 |
| AENWADNEPNNKRNNED | 463 |
| RKNNKTWTWVGTKKALTNE | 464 |
| KKALTNEAENWAD | 465 |
| CQXRYTDLVAIQNKXE | 466 |
| RKXNXXWTWVGTXKXLTEE | 467 |
| AENWADGEPNNKXNXED | 468 |
| CXXXYTXLVAIQNKXE | 469 |
| RKXXXXWXWVGTXKXLTXE | 470 |
| AXNWXXXEPNNXXXED | 471 |
| XKXKTXEAXNWXX | 472 |

Table 11—Antipathogenic peptide sequences

| Sequence/structure | SEQ ID NO: |
|------------------------------------|------------|
| GFFALIPKIISSPLFKTLLSAVGSALSSSSGGQQ | 503 |
| GFFALIPKIISSPLFKTLLSAVGSALSSSSGGQE | 504 |
| GFFALIPKIISSPLFKTLLSAV | 505 |
| GFFALIPKIISSPLFKTLLSAV | 506 |
| KGFFALIPKIISSPLFKTLLSAV | 507 |
| KKGFFALIPKIISSPLFKTLLSAV | 508 |
| KKGFFALIPKIISSPLFKTLLSAV | 509 |
| GFFALIPKIIS | 510 |
| GIGAVLKVLTTGLPALISWIKRKRQQ | 511 |
| GIGAVLKVLTTGLPALISWIKRKRQQ | 512 |
| GIGAVLKVLTTGLPALISWIKRKRQQ | 513 |
| GIGAVLKVLTTGLPALISWIKR | 514 |
| AVLKVLTTGLPALISWIKR | 515 |
| KLLLLLKLLLLK | 516 |
| KLLKLLKLLK | 517 |
| KLLKLLKLLK | 518 |
| KKLLKLLKLLK | 519 |
| KLLKLLKLLK | 520 |
| KLLKLLKLLK | 521 |
| KLLLK | 522 |
| KLLKLLK | 523 |
| KLLKLLKLLK | 524 |
| KLLKLLKLLK | 525 |
| KLLKLLKLLK | 526 |
| KAAAKAAAKAAK | 527 |
| KVVVKVVVKVVK | 528 |
| KVVVKVVVKVVK | 529 |
| KVVVKVVVKVVK | 530 |
| KVVVKVVVKVVK | 531 |
| KLILKL | 532 |
| KVLHLL | 533 |
| LKLRL | 534 |
| KPLHLL | 535 |
| KLILKLVR | 536 |
| KVFHLLHL | 537 |
| HKFRILKL | 538 |
| KPFHILHL | 539 |
| KIIKIKIKIK | 540 |
| KIIKIKIKIK | 541 |
| KIIKIKIKIK | 542 |
| KIPKIKIKIPK | 543 |
| KIPKIKIKIVK | 544 |
| RIIRIRIRIR | 545 |
| RIIRIRIRIR | 546 |
| RIIRIRIRIR | 547 |
| RIVIRIRIRLIR | 548 |

| | |
|------------------------------------|-----|
| RIIVRIRLRIIR | 549 |
| RIGIRLVRRIIR | 550 |
| KIVIRIRIRLIR | 551 |
| RIAVKWRLRFIK | 552 |
| KIGWKLRVRIIR | 553 |
| KKIGWLIIRVRR | 554 |
| RIVIRIRIRLIRIR | 555 |
| RIIVRIRLRIIRVR | 556 |
| RIGIRLVRRIIRRV | 557 |
| KIVIRIRARLIRIRIR | 558 |
| RIIVKIRLRIIKKIRL | 559 |
| KIGIKARVRIIRVKII | 560 |
| RIIVHIRLRIIHHIRL | 561 |
| HIGIKAHVRIIRVHII | 562 |
| RIYVKIHLRYIKKIRL | 563 |
| KIGHKARVHIIRYKII | 564 |
| RIYVKPHPRYIKKIRL | 565 |
| KPGHKARPHIIRYKII | 566 |
| KIVIRIRIRLIRIRIRKIV | 567 |
| RIIVKIRLRIIKKIRLIKK | 568 |
| KIGWKLRVRIIRVKIGRLR | 569 |
| KIVIRIRIRLIRIRIRKIVKVKRIR | 570 |
| RFAVKIRLRIIKKIRLIKKIRKRVIK | 571 |
| KAGWKLRVRIIRVKIGRLRKIGWKKRVRIK | 572 |
| RIYVKPHPRYIKKIRL | 573 |
| KPGHKARPHIIRYKII | 574 |
| KIVIRIRIRLIRIRIRKIV | 575 |
| RIIVKIRLRIIKKIRLIKK | 576 |
| RIYVSKISYIKKIRL | 577 |
| KIVIFTRIRLTSIRIRSIV | 578 |
| KPIHKARPTIIRYKMI | 579 |
| cyclicCKGFFALIPKIISSPLFKTLLSAVC | 580 |
| CKKGFFALIPKIISSPLFKTLLSAVC | 581 |
| CKKKGFFALIPKIISSPLFKTLLSAVC | 582 |
| CyclicCRIVIRIRIRLIRIRC | 583 |
| CyclicCKPGHKARPHIIRYKIIC | 584 |
| CyclicCRFAVKIRLRIIKKIRLIKKIRKRVIKC | 585 |
| KLLKLLK KLLKC | 586 |
| KLLKLLKLLK | 587 |
| KLLKLLKLLKLLKC | 588 |
| KLLKLLKLLKLLK | 589 |

Table 12—VIP-mimetic peptide sequences

| Sequence/structure | SEQ ID NO: |
|--|------------|
| HSDAVFYDNYTR LRKQMAVKKYLN SILN | 590 |
| Nle HSDAVFYDNYTR LRKQMAVKKYLN SILN | 591 |
| X ₁ X ₁ ' X ₁ " X ₂ | 592 |
| X ₂ S X ₄ LN | 593 |
| NH CH CO KKYX5 NH CH CO X6 <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> $\begin{array}{c} \\ (\text{CH}_2)_m \end{array}$ </div> <div style="text-align: center;">Z</div> <div style="text-align: center;"> $\begin{array}{c} \\ (\text{CH}_2)_n \end{array}$ </div> </div> | 594 |
| KKYL | 595 |
| NSILN | 596 |
| KKYL | 597 |
| KKYA | 598 |
| AVKKYL | 599 |
| NSILN | 600 |
| KKYV | 601 |
| SILauN | 602 |
| KKYLNle | 603 |
| NSYLN | 604 |
| NSIYN | 605 |
| KKYLPPNSILN | 606 |
| LauKKYL | 607 |
| CapKKYL | 608 |
| KYL | NR |
| KKYNle | 609 |
| VKKYL | 610 |
| LNSILN | 611 |
| YLNSILN | 612 |
| KKYLN | 613 |
| KKYLNS | 614 |
| KKYLNSI | 615 |
| KKYLNSIL | 616 |
| KKYL | 617 |
| KKYDA | 618 |
| AVKKYL | 619 |
| NSILN | 620 |
| KKYV | 621 |
| SILauN | 622 |
| NSYLN | 623 |
| NSIYN | 624 |
| KKYLNle | 625 |
| KKYLPPNSILN | 626 |
| KKYL | 627 |
| KKYDA | 628 |
| AVKKYL | 629 |
| NSILN | 630 |
| KKYV | 631 |
| SILauN | 632 |

| | |
|---|-----|
| LauKKYL | 633 |
| CapKKYL | 634 |
| KYL | NR |
| KYL | NR |
| KKYNIe | 635 |
| VKKYL | 636 |
| LNSILN | 637 |
| YLNSILN | 638 |
| KKYLNie | 639 |
| KKYLN | 640 |
| KKYLNS | 641 |
| KKYLNSI | 642 |
| KKYLNSIL | 643 |
| KKKYLD | 644 |
| cyclicCKKYLC | 645 |
| CKKYLK S-CH ₂ -CO | 646 |
| KKYA | 647 |
| WWTDTGLW | 648 |
| WWTDDGLW | 649 |
| WWDTRGLWVWTI | 650 |
| FWGNDGIWLESG | 651 |
| DWDQFGLWRGAA | 652 |
| RWDDNGLWVVVL | 653 |
| SGMWSHYGIWMG | 654 |
| GGRWDQAGLWVA | 655 |
| KLWSEQGIWMGE | 656 |
| CWSMHGLWLC | 657 |
| GCWDNTGIWVPC | 658 |
| DWDTRGLWVY | 659 |
| SLWDENGAWI | 660 |
| KWDDRGLWMH | 661 |
| QAWNERGLWT | 662 |
| QWDTRGLWVA | 663 |
| WNVHGIWQE | 664 |
| SWDTRGLWVE | 665 |
| DWDTRGLWVA | 666 |
| SWGRDGLWIE | 667 |
| EWTDNGLWAL | 668 |
| SWDEKGLWSA | 669 |
| SWDSSGLWMD | 670 |

Table 13—Mdm/hdm antagonist peptide sequences

| Sequence/structure | SEQ ID NO: |
|--------------------|------------|
| TFSDLW | 130 |
| QETFSDLWKLLP | 131 |
| QPTFSDLWKLLP | 132 |
| QETFSDYWKLLP | 133 |
| QPTFSDYWKLLP | 134 |
| MPRFMDYWEGLN | 135 |
| VQNFIDYWTQQF | 136 |
| TGPAFTHYWATF | 137 |
| IDRPTFRDHWFALV | 138 |
| PRPALVFADYWETLY | 139 |
| PAFSRFWSDLSAGAH | 140 |
| PAFSRFWSKLSAGAH | 141 |
| PXFXDYWXXL | 142 |
| QETFSDLWKLLP | 143 |
| QPTFSDLWKLLP | 144 |
| QETFSDYWKLLP | 145 |
| QPTFSDYWKLLP | 146 |

Table 14—Calmodulin antagonist peptide sequences

| Sequence/structure | SEQ ID NO: |
|-----------------------|------------|
| SCVKWGGKEFCGS | 164 |
| SCWKYWGKECGS | 165 |
| SCYEWGKLRWCGS | 166 |
| SCLRWGKWSNCGS | 167 |
| SCWRWGKYQICGS | 168 |
| SCVSWGALKLCGS | 169 |
| SCIRWGQNTFCGS | 170 |
| SCWQWGNLKICGS | 171 |
| SCVRWGQLSICGS | 172 |
| LKKFNARRKLKGAILTTMLAK | 173 |
| RRWKKNFIAVSAANRFKK | 174 |
| RKWQKTGHAVRAIGRLSS | 175 |
| INLKALAALAKKIL | 176 |
| KIWSILAPLGTTLVKLVA | 177 |
| LKKLLKLLKKLLKL | 178 |
| LKWKKLLKLLKKLLKKLL | 179 |
| AEWPSLTEIKTLSHFSV | 180 |
| AEWPSPTRVISTTYFGS | 181 |
| AELAHWPPVKTVLRSFT | 182 |
| AEGSWLQLLNLMKQMNN | 183 |
| AEWPSLTEIK | 184 |

**Table 15—Mast cell antagonists/Mast cell protease inhibitor
peptide sequences**

| Sequence/structure | SEQ ID NO: |
|---------------------------|-----------------------|
| SGSGVLKRPLPILPVTR | 272 |
| RWLSSRPLPPLPLPPRT | 273 |
| GSGSYDTLALPSLPLHPMSS | 274 |
| GSGSYDTRALPSLPLHPMSS | 275 |
| GSGSSGVTMYPKLPPHWSMA | 276 |
| GSGSSGVRMYPKLPPHWSMA | 277 |
| GSGSSSMRMVPTIPGSAKHG | 278 |
| RNR | NR |
| QT | NR |
| RQK | NR |
| NRQ | NR |
| RQK | NR |
| RNRQKT | 436 |
| RNRQ | 437 |
| RNRQK | 438 |
| NRQKT | 439 |
| RQKT | 440 |

Table 16—SH3 antagonist peptide sequences

| Sequence/structure | SEQ ID NO: |
|-----------------------------|------------|
| RPLPPLP | 282 |
| RELPPPLP | 283 |
| SPLPPLP | 284 |
| GPLPPLP | 285 |
| RPLPIPP | 286 |
| RPLPIPP | 287 |
| RRLPPTP | 288 |
| RQLPPTP | 289 |
| RPLPSRP | 290 |
| RPLPTRP | 291 |
| SRLPPLP | 292 |
| RALPSPP | 293 |
| RRLP RTP | 294 |
| RPVPPIT | 295 |
| ILAPPVP | 296 |
| RPLPMLP | 297 |
| RPLPILP | 298 |
| RPLPSLP | 299 |
| RPLPSLP | 300 |
| RPLPMIP | 301 |
| RPLPLIP | 302 |
| RPLPPTP | 303 |
| RSLPPLP | 304 |
| RPQPPPP | 305 |
| RQLPIPP | 306 |
| XXXRPLPPLXP | 307 |
| XXXRPLPPIPXX | 308 |
| XXXRPLPPLPXX | 309 |
| RXXRPLPPLXP | 310 |
| RXXRPLPPLPPP | 311 |
| PPPYPPPIPXX | 312 |
| PPPYPPPPVPXX | 313 |
| LXXRPLPX Ψ P | 314 |
| Ψ XXRPLPXL | 315 |
| PPX Θ XPPP Ψ P | 316 |
| +PP Ψ PXKXPWL | 317 |
| RPX Ψ P Ψ R+SXP | 318 |
| PPVPPRPXXTL | 319 |
| Ψ P Ψ LP Ψ K | 320 |
| + Θ DXPLPXL | 321 |

Table 17—Somatostatin or cortistatin mimetic peptide sequences

| Sequence/structure | SEQ ID NO: |
|--|------------|
| X ¹ -X ² -Asn-Phe-Phe-Trp-Lys-Thr-Phe-X ³ -Ser-X ⁴ | 473 |
| Asp Arg Met Pro Cys Arg Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys Lys | 474 |
| Met Pro Cys Arg Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys Lys | 475 |
| Cys Arg Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys Lys | 476 |
| Asp Arg Met Pro Cys Arg Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys | 477 |
| Met Pro Cys Arg Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys | 478 |
| Cys Arg Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys | 479 |
| Asp Arg Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys | 480 |
| Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys Lys | 481 |
| Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys Lys | 482 |
| Asp Arg Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys | 483 |
| Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys | 484 |
| Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys | 485 |
| Asp Arg Met Pro Cys Arg Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys Lys | 486 |
| Met Pro Cys Arg Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys Lys | 487 |
| Cys Arg Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys Lys | 488 |
| Asp Arg Met Pro Cys Arg Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys | 489 |
| Met Pro Cys Arg Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys | 490 |
| Cys Arg Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys | 491 |
| Asp Arg Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys Lys | 492 |
| Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys Lys | 493 |
| Cys Lys Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys Lys | 494 |
| Asp Arg Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys | 495 |
| Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys | 496 |
| Cys Lys Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys | 497 |

Table 18—UKR antagonist peptide sequences

| Sequence/structure | SEQ ID NO: |
|--------------------|---------------|
| AEPMPHSLNFSQYLWYT | 196 |
| AEHTYSSLWDTYSPLAF | 197 |
| AELDLWMRHYPLSFSNR | 198 |
| AESSLWTRYAWPSMPSY | 199 |
| AEWHPGLSFGSYLWSKT | 200 |
| AEPALLNWSFFFNPGLH | 201 |
| AEWSFYNLHLPEPQTIF | 202 |
| AEPLDLWSLYSLPPLAM | 203 |
| AEPTLWQLYQFPLRLSG | 204 |
| AEISFSELMWLRSTPAF | 205 |
| AELSEADLWTTWFGMGS | 206 |
| AESSLWRIFSPSALMMS | 207 |
| AESLPTLTSILWGKESV | 208 |
| AETLFMDLWHDKHILLT | 209 |
| AEILNFPLWHEPLWSTE | 210 |
| AESQTGTLNTLFWNTLR | 211 |
| AEPVYQYELDSYLRSY | 430 |
| AELDLSTFYDIQYLLRT | 431 |
| AEFFKLGPNGYVYLHSA | 432 |
| FKLXXXGYVYL | 433 |
| AESTYHHLSLGYMYTLN | 434 |
| YHXLXXGYMYT | 435 |

**Table 19—Macrophage and/or
T-cell inhibiting peptide sequences**

| Sequence/structure | SEQ ID NO: |
|---------------------------|-----------------------|
| Xaa-Yaa-Arg | NR |
| Arg-Yaa-Xaa | NR |
| Xaa-Arg-Yaa | NR |
| Yaa-Arg-Xaa | NR |
| Ala-Arg | NR |
| Arg-Arg | NR |
| Asn-Arg | NR |
| Asp-Arg | NR |
| Cys-Arg | NR |
| Gln-Arg | NR |
| Glu-Arg | NR |
| Gly-Arg | NR |
| His-arg | NR |
| Ile-Arg | NR |
| Leu-Arg | NR |
| Lys-Arg | NR |
| Met-Arg | NR |
| Phe-Arg | NR |
| Ser-Arg | NR |
| Thr-Arg | NR |
| Trp-Arg | NR |
| Tyr-Arg | NR |
| Val-Arg | NR |
| Ala-Glu-Arg | NR |
| Arg-Glu-Arg | NR |
| Asn-Glu-Arg | NR |
| Asp-Glu-Arg | NR |
| Cys-Glu-Arg | NR |
| Gln-Glu-Arg | NR |
| Glu-Glu-Arg | NR |
| Gly-Glu-Arg | NR |
| His-Glu-Arg | NR |
| Ile-Glu-Arg | NR |
| Leu-Glu-Arg | NR |
| Lys-Glu-Arg | NR |
| Met-Glu-Arg | NR |
| Phe-Glu-Arg | NR |
| Pro-Glu-Arg | NR |
| Ser-Glu-Arg | NR |
| Thr-Glu-Arg | NR |
| Trp-Glu-Arg | NR |
| Tyr-Glu-Arg | NR |
| Val-Glu-Arg | NR |

| | |
|-------------|----|
| Arg-Ala | NR |
| Arg-Asp | NR |
| Arg-Cys | NR |
| Arg-Gln | NR |
| Arg-Glu | NR |
| Arg-Gly | NR |
| Arg-His | NR |
| Arg-Ile | NR |
| Arg-Leu | NR |
| Arg-Lys | NR |
| Arg-Met | NR |
| Arg-Phe | NR |
| Arg-Pro | NR |
| Arg-Ser | NR |
| Arg-Thr | NR |
| Arg-Trp | NR |
| Arg-Tyr | NR |
| Arg-Val | NR |
| Arg-Glu-Ala | NR |
| Arg-Glu-Asn | NR |
| Arg-Glu-Asp | NR |
| Arg-Glu-Cys | NR |
| Arg-Glu-Gln | NR |
| Arg-Glu-Glu | NR |
| Arg-Glu-Gly | NR |
| Arg-Glu-His | NR |
| Arg-Glu-Ile | NR |
| Arg-Glu-Leu | NR |
| Arg-Glu-Lys | NR |
| Arg-Glu-Met | NR |
| Arg-Glu-Phe | NR |
| Arg-Glu-Pro | NR |
| Arg-Glu-Ser | NR |
| Arg-Glu-Thr | NR |
| Arg-Glu-Trp | NR |
| Arg-Glu-Tyr | NR |
| Arg-Glu-Val | NR |
| Ala-Arg-Glu | NR |
| Arg-Arg-Glu | NR |
| Asn-Arg-Glu | NR |
| Asp-Arg-Glu | NR |
| Cys-Arg-Glu | NR |
| Gln-Arg-Glu | NR |
| Glu-Arg-Glu | NR |
| Gly-Arg-Glu | NR |
| His-Arg-Glu | NR |
| Ile-Arg-Glu | NR |
| Leu-Arg-Glu | NR |
| Lys-Arg-Glu | NR |
| Met-Arg-Glu | NR |

| | |
|--------------|----|
| Phe-Arg-Glu | NR |
| Pro-Arg-Glu | NR |
| Ser-Arg-Glu | NR |
| Thr-Arg-Glu | NR |
| Trp-Arg-Glu | NR |
| Tyr-Arg-Glu | NR |
| Val-Arg-Glu | NR |
| Glu-Arg-Ala, | NR |
| Glu-Arg-Arg | NR |
| Glu-Arg-Asn | NR |
| Glu-Arg-Asp | NR |
| Glu-Arg-Cys | NR |
| Glu-Arg-Gln | NR |
| Glu-Arg-Gly | NR |
| Glu-Arg-His | NR |
| Glu-Arg-Ile | NR |
| Glu-Arg-Leu | NR |
| Glu-Arg-Lys | NR |
| Glu-Arg-Met | NR |
| Glu-Arg-Phe | NR |
| Glu-Arg-Pro | NR |
| Glu-Arg-Ser | NR |
| Glu-Arg-Thr | NR |
| Glu-Arg-Trp | NR |
| Glu-Arg-Tyr | NR |
| Glu-Arg-Val | NR |

Table 20—Additional Exemplary Pharmacologically Active Peptides

| Sequence/structure | SEQ ID NO: | Activity |
|------------------------------------|------------|------------------------------------|
| VEPNCDIHVMWEWECFERL | 1027 | VEGF-antagonist |
| GERWCDFDGLTWVCGEES | 1084 | VEGF-antagonist |
| RGWVEICVADDNGMCVTEAQ | 1085 | VEGF-antagonist |
| GWDECDVARMWEWECFAGV | 1086 | VEGF- antagonist |
| GERWCDFDGPRAWVCGWEI | 501 | VEGF- antagonist |
| EELWCDFDGPRAWVCGYVK | 502 | VEGF- antagonist |
| RGWVEICAADDYGRCLTEAQ | 1031 | VEGF- antagonist |
| RGWVEICESDVWGRCL | 1087 | VEGF- antagonist |
| RGWVEICESDVWGRCL | 1088 | VEGF- antagonist |
| GGNECDIARMWEWECFERL | 1089 | VEGF- antagonist |
| RGWVEICAADDYGRCL | 1090 | VEGF-antagonist |
| CTTHWGF TLC | 1028 | MMP inhibitor |
| CLRSGXGC | 1091 | MMP inhibitor |
| CXXHWGFXXC | 1092 | MMP inhibitor |
| CXPXC | 1093 | MMP inhibitor |
| CRRHWGF EFC | 1094 | MMP inhibitor |
| STTHWGF TLS | 1095 | MMP inhibitor |
| CSLHWGF WWC | 1096 | CTLA4-mimetic |
| GFVCSGIFAVGVGRG | 125 | CTLA4-mimetic |
| APGVRLGCAVLGRYC | 126 | CTLA4-mimetic |
| LLGRMK | 105 | Antiviral (HBV) |
| ICVVQDWGHHRCTAGHMANLTSHASAI | 127 | C3b antagonist |
| ICVVQDWGHHRCT | 128 | C3b antagonist |
| CVVQDWGH HAC | 129 | C3b antagonist |
| STGGFDDVYDWARGVSSALTTTLVATR | 185 | Vinculin-binding |
| STGGFDDVYDWARRVSSALTTTLVATR | 186 | Vinculin-binding |
| SRGVNFSEWLYDMSAAMKEASNVP SRRSR | 187 | Vinculin-binding |
| SSQNWDMEAGVEDLTAAMLGLLSTIHSSSR | 188 | Vinculin-binding |
| SSPSLYTQFLVNYESAATRIQDLLIASRPSR | 189 | Vinculin-binding |
| SSTGWVDLLGALQRAADATRTSIPPSLQNSR | 190 | Vinculin-binding |
| DVYTKKELIECARRVSEK | 191 | Vinculin-binding |
| EKGSYYPGSGIAQFHIDYNNVS | 192 | C4BP-binding |
| SGIAQFHIDYNNVSSAEGWHVN | 193 | C4BP-binding |
| LVTVEKGSYYPGSGIAQFHIDYNNVSSAEGWHVN | 194 | C4BP-binding |
| SGIAQFHIDYNNVS | 195 | C4BP-binding |
| LLGRMK | 279 | anti-HBV |
| ALLGRMKG | 280 | anti-HBV |
| LDPAFR | 281 | anti-HBV |
| CXXRGDC | 322 | Inhibition of platelet aggregation |
| RPLPPLP | 323 | Src antagonist |
| PPVPPR | 324 | Src antagonist |
| XFXDXWXXLXX | 325 | Anti-cancer (particularly for |

| | | |
|--|------|-------------------------------------|
| | | sarcomas) |
| KACRRLLFGPVDSEQLSRDCD | 326 | p16-mimetic |
| RERWNFDVFTETPLEGDFAW | 327 | p16-mimetic |
| KRRQTSMTDFYHSKRRLIFS | 328 | p16-mimetic |
| TSMTDFYHSKRRLIFSKRKP | 329 | p16-mimetic |
| RRLIF | 330 | p16-mimetic |
| KRRQTSATDFYHSKRRLIFSRQIKIWFQNRRMKWKK | 331 | p16-mimetic |
| KRRLIFSKRQIKIWFQNRRMKWKK | 332 | p16-mimetic |
| Asn Gln Gly Arg His Phe Cys Gly Gly Ala Leu Ile His Ala Arg Phe Val Met Thr Ala Ala Ser Cys Phe Gln | 498 | CAP37 mimetic/LPS binding |
| Arg His Phe Cys Gly Gly Ala Leu Ile His Ala Arg Phe Val Met Thr Ala Ala Ser Cys | 499 | CAP37 mimetic/LPS binding |
| Gly Thr Arg Cys Gln Val Ala Gly Trp Gly Ser Gln Arg Ser Gly Gly Arg Leu Ser Arg Phe Pro Arg Phe Val Asn Val | 500 | CAP37 mimetic/LPS binding |
| WHWRHRIPLQLAAGR | 1097 | carbohydrate (GD1 alpha) mimetic |
| LKTPRV | 1098 | β 2GPI Ab binding |
| NLTKTPRV | 1099 | β 2GPI Ab binding |
| NLTKTPRVGGC | 1100 | β 2GPI Ab binding |
| KDKATF | 1101 | β 2GPI Ab binding |
| KDKATFGCHD | 1102 | β 2GPI Ab binding |
| KDKATFGCHDGC | 1103 | β 2GPI Ab binding |
| TLRVYK | 1104 | β 2GPI Ab binding |
| ATLRVYKGG | 1105 | β 2GPI Ab binding |
| CATLRVYKGG | 1106 | β 2GPI Ab binding |
| INLKALAALAKKIL | 1107 | Membrane- transporting |
| GWT | NR | Membrane- transporting |
| GWTLSAGYLLG | 1108 | Membrane- transporting |
| GWTLSAGYLLGKINLKALAALAKKIL | 1109 | Membrane- transporting |

The present invention is also particularly useful with peptides having activity in treatment of:

- cancer, wherein the peptide is a VEGF-mimetic or a VEGF receptor antagonist, a HER2 agonist or antagonist, a CD20 antagonist and the like;
- asthma, wherein the protein of interest is a CKR3 antagonist, an IL-5 receptor antagonist, and the like;
- thrombosis, wherein the protein of interest is a GPIIb antagonist, a GPIIIa antagonist, and the like;

- autoimmune diseases and other conditions involving immune modulation, wherein the protein of interest is an IL-2 receptor antagonist, a CD40 agonist or antagonist, a CD40L agonist or antagonist, a thymopoietin mimetic and the like.

5 Vehicles. This invention requires the presence of at least one vehicle (F^1 , F^2) attached to a peptide through the N-terminus, C-terminus or a sidechain of one of the amino acid residues. Multiple vehicles may also be used; e.g., Fc's at each terminus or an Fc at a terminus and a PEG group at the other terminus or a sidechain.

10 An Fc domain is the preferred vehicle. The Fc domain may be fused to the N or C termini of the peptides or at both the N and C termini. For the TPO-mimetic peptides, molecules having the Fc domain fused to the N terminus of the peptide portion of the molecule are more bioactive than other such fusions, so fusion to the N terminus is preferred.

15 As noted above, Fc variants are suitable vehicles within the scope of this invention. A native Fc may be extensively modified to form an Fc variant in accordance with this invention, provided binding to the salvage receptor is maintained; see, for example WO 97/34631 and WO 96/32478. In such Fc variants, one may remove one or more sites of a native Fc that
20 provide structural features or functional activity not required by the fusion molecules of this invention. One may remove these sites by, for example, substituting or deleting residues, inserting residues into the site, or truncating portions containing the site. The inserted or substituted residues may also be altered amino acids, such as peptidomimetics or D-
25 amino acids. Fc variants may be desirable for a number of reasons, several of which are described below. Exemplary Fc variants include molecules and sequences in which:

1. Sites involved in disulfide bond formation are removed. Such removal may avoid reaction with other cysteine-containing proteins present in

the host cell used to produce the molecules of the invention. For this purpose, the cysteine-containing segment at the N-terminus may be truncated or cysteine residues may be deleted or substituted with other amino acids (e.g., alanyl, seryl). In particular, one may truncate the N-terminal 20-amino acid segment of SEQ ID NO: 2 or delete or
5 substitute the cysteine residues at positions 7 and 10 of SEQ ID NO: 2. Even when cysteine residues are removed, the single chain Fc domains can still form a dimeric Fc domain that is held together non-covalently.

2. A native Fc is modified to make it more compatible with a selected host
10 cell. For example, one may remove the PA sequence near the N-terminus of a typical native Fc, which may be recognized by a digestive enzyme in E. coli such as proline iminopeptidase. One may also add an N-terminal methionine residue, especially when the molecule is expressed recombinantly in a bacterial cell such as E. coli. The Fc
15 domain of SEQ ID NO: 2 (Figure 4) is one such Fc variant.
3. A portion of the N-terminus of a native Fc is removed to prevent N-terminal heterogeneity when expressed in a selected host cell. For this purpose, one may delete any of the first 20 amino acid residues at the N-terminus, particularly those at positions 1, 2, 3, 4 and 5.
- 20 4. One or more glycosylation sites are removed. Residues that are typically glycosylated (e.g., asparagine) may confer cytolytic response. Such residues may be deleted or substituted with unglycosylated residues (e.g., alanine).
5. Sites involved in interaction with complement, such as the C1q binding
25 site, are removed. For example, one may delete or substitute the EKK sequence of human IgG1. Complement recruitment may not be advantageous for the molecules of this invention and so may be avoided with such an Fc variant.

6. Sites are removed that affect binding to Fc receptors other than a salvage receptor. A native Fc may have sites for interaction with certain white blood cells that are not required for the fusion molecules of the present invention and so may be removed.
- 5 7. The ADCC site is removed. ADCC sites are known in the art; see, for example, Molec. Immunol. 29 (5): 633-9 (1992) with regard to ADCC sites in IgG1. These sites, as well, are not required for the fusion molecules of the present invention and so may be removed.
- 10 8. When the native Fc is derived from a non-human antibody, the native Fc may be humanized. Typically, to humanize a native Fc, one will substitute selected residues in the non-human native Fc with residues that are normally found in human native Fc. Techniques for antibody humanization are well known in the art.

Preferred Fc variants include the following. In SEQ ID NO: 2 (Figure 4) the leucine at position 15 may be substituted with glutamate; the glutamate at position 99, with alanine; and the lysines at positions 101 and 103, with alanines. In addition, one or more tyrosine residues can be replaced by phenylalanine residues.

An alternative vehicle would be a protein, polypeptide, peptide, antibody, antibody fragment, , or small molecule (e.g., a peptidomimetic compound) capable of binding to a salvage receptor. For example, one could use as a vehicle a polypeptide as described in U.S. Pat. No. 5,739,277, issued April 14, 1998 to Presta et al. Peptides could also be selected by phage display for binding to the FcRn salvage receptor. Such salvage receptor-binding compounds are also included within the meaning of "vehicle" and are within the scope of this invention. Such vehicles should be selected for increased half-life (e.g., by avoiding sequences recognized by proteases) and decreased immunogenicity (e.g., by favoring non-immunogenic sequences, as discovered in antibody humanization).

As noted above, polymer vehicles may also be used for F¹ and F². Various means for attaching chemical moieties useful as vehicles are currently available, see, e.g., Patent Cooperation Treaty ("PCT") International Publication No. WO 96/11953, entitled "N-Terminally Chemically Modified Protein Compositions and Methods," herein
5 incorporated by reference in its entirety. This PCT publication discloses, among other things, the selective attachment of water soluble polymers to the N-terminus of proteins.

A preferred polymer vehicle is polyethylene glycol (PEG). The PEG
10 group may be of any convenient molecular weight and may be linear or branched. The average molecular weight of the PEG will preferably range from about 2 kiloDalton ("kD") to about 100 kDa, more preferably from about 5 kDa to about 50 kDa, most preferably from about 5 kDa to about 10 kDa. The PEG groups will generally be attached to the compounds of
15 the invention via acylation or reductive alkylation through a reactive group on the PEG moiety (e.g., an aldehyde, amino, thiol, or ester group) to a reactive group on the inventive compound (e.g., an aldehyde, amino, or ester group).

A useful strategy for the PEGylation of synthetic peptides consists
20 of combining, through forming a conjugate linkage in solution, a peptide and a PEG moiety, each bearing a special functionality that is mutually reactive toward the other. The peptides can be easily prepared with conventional solid phase synthesis (see, for example, Figures 5 and 6 and the accompanying text herein). The peptides are "preactivated" with an
25 appropriate functional group at a specific site. The precursors are purified and fully characterized prior to reacting with the PEG moiety. Ligation of the peptide with PEG usually takes place in aqueous phase and can be easily monitored by reverse phase analytical HPLC. The PEGylated peptides can be easily purified by preparative HPLC and characterized by

analytical HPLC, amino acid analysis and laser desorption mass spectrometry.

Polysaccharide polymers are another type of water soluble polymer which may be used for protein modification. Dextrans are polysaccharide polymers comprised of individual subunits of glucose predominantly
5 linked by α 1-6 linkages. The dextran itself is available in many molecular weight ranges, and is readily available in molecular weights from about 1 kD to about 70 kD. Dextran is a suitable water soluble polymer for use in the present invention as a vehicle by itself or in combination with another
10 vehicle (e.g., Fc). See, for example, WO 96/11953 and WO 96/05309. The use of dextran conjugated to therapeutic or diagnostic immunoglobulins has been reported; see, for example, European Patent Publication No. 0 315 456, which is hereby incorporated by reference. Dextran of about 1 kD to about 20 kD is preferred when dextran is used as a vehicle in
15 accordance with the present invention.

Linkers. Any "linker" group is optional. When present, its chemical structure is not critical, since it serves primarily as a spacer. The linker is preferably made up of amino acids linked together by peptide bonds. Thus, in preferred embodiments, the linker is made up of from 1 to 20
20 amino acids linked by peptide bonds, wherein the amino acids are selected from the 20 naturally occurring amino acids. Some of these amino acids may be glycosylated, as is well understood by those in the art. In a more preferred embodiment, the 1 to 20 amino acids are selected from glycine, alanine, proline, asparagine, glutamine, and lysine. Even more preferably,
25 a linker is made up of a majority of amino acids that are sterically unhindered, such as glycine and alanine. Thus, preferred linkers are polyglycines (particularly (Gly)₄, (Gly)₅), poly(Gly-Ala), and polyalanines. Other specific examples of linkers are:

(Gly)₃Lys(Gly)₄ (SEQ ID NO: 333);

(Gly)₃AsnGlySer(Gly)₂ (SEQ ID NO: 334);

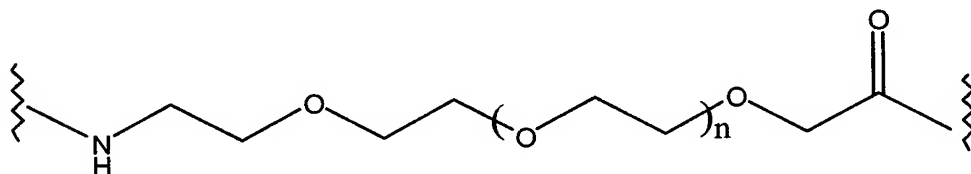
(Gly)₃Cys(Gly)₄ (SEQ ID NO: 335); and

GlyProAsnGlyGly (SEQ ID NO: 336).

To explain the above nomenclature, for example, (Gly)₃Lys(Gly)₄ means
 5 Gly-Gly-Gly-Lys-Gly-Gly-Gly-Gly. Combinations of Gly and Ala are also preferred. The linkers shown here are exemplary; linkers within the scope of this invention may be much longer and may include other residues.

Non-peptide linkers are also possible. For example, alkyl linkers such as -NH-(CH₂)_s-C(O)-, wherein s = 2-20 could be used. These alkyl
 10 linkers may further be substituted by any non-sterically hindering group such as lower alkyl (e.g., C₁-C₆) lower acyl, halogen (e.g., Cl, Br), CN, NH₂, phenyl, etc. An exemplary non-peptide linker is a PEG linker,

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15

wherein n is such that the linker has a molecular weight of 100 to 5000 kD, preferably 100 to 500 kD. The peptide linkers may be altered to form derivatives in the same manner as described above.

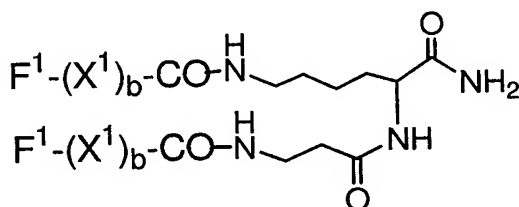
Derivatives. The inventors also contemplate derivatizing the
 20 peptide and/or vehicle portion of the compounds. Such derivatives may improve the solubility, absorption, biological half life, and the like of the compounds. The moieties may alternatively eliminate or attenuate any undesirable side-effect of the compounds and the like. Exemplary derivatives include compounds in which:

- 25 1. The compound or some portion thereof is cyclic. For example, the peptide portion may be modified to contain two or more Cys residues (e.g., in the linker), which could cyclize by disulfide bond formation.

For citations to references on preparation of cyclized derivatives, see Table 2.

2. The compound is cross-linked or is rendered capable of cross-linking between molecules. For example, the peptide portion may be modified to contain one Cys residue and thereby be able to form an intermolecular disulfide bond with a like molecule. The compound may also be cross-linked through its C-terminus, as in the molecule shown below.

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3. One or more peptidyl [-C(O)NR-] linkages (bonds) is replaced by a non-peptidyl linkage. Exemplary non-peptidyl linkages are -CH₂-carbamate [-CH₂-OC(O)NR-], phosphonate, -CH₂-sulfonamide [-CH₂-S(O)₂NR-], urea [-NHC(O)NH-], -CH₂-secondary amine, and alkylated peptide [-C(O)NR⁶- wherein R⁶ is lower alkyl].
4. The N-terminus is derivatized. Typically, the N-terminus may be acylated or modified to a substituted amine. Exemplary N-terminal derivative groups include -NRR¹ (other than -NH₂), -NRC(O)R¹, -NRC(O)OR¹, -NRS(O)₂R¹, -NHC(O)NHR¹, succinimide, or benzyloxycarbonyl-NH- (CBZ-NH-), wherein R and R¹ are each independently hydrogen or lower alkyl and wherein the phenyl ring may be substituted with 1 to 3 substituents selected from the group consisting of C₁-C₄ alkyl, C₁-C₄ alkoxy, chloro, and bromo.
5. The free C-terminus is derivatized. Typically, the C-terminus is esterified or amidated. For example, one may use methods described in the art to add (NH-CH₂-CH₂-NH₂)₂ to compounds of this invention

having any of SEQ ID NOS: 504 to 508 at the C-terminus. Likewise, one may use methods described in the art to add $-NH_2$ to compounds of this invention having any of SEQ ID NOS: 924 to 955, 963 to 972, 1005 to 1013, or 1018 to 1023 at the C-terminus. Exemplary C-terminal derivative groups include, for example, $-C(O)R^2$ wherein R^2 is lower alkoxy or $-NR^3R^4$ wherein R^3 and R^4 are independently hydrogen or C_1 - C_8 alkyl (preferably C_1 - C_4 alkyl).

7. A disulfide bond is replaced with another, preferably more stable, cross-linking moiety (e.g., an alkylene). See, e.g., Bhatnagar *et al.* (1996), *J. Med. Chem.* 39: 3814-9; Alberts *et al.* (1993) *Thirteenth Am. Pep. Symp.*, 357-9.

8. One or more individual amino acid residues is modified. Various derivatizing agents are known to react specifically with selected sidechains or terminal residues, as described in detail below.

Lysinyl residues and amino terminal residues may be reacted with succinic or other carboxylic acid anhydrides, which reverse the charge of the lysinyl residues. Other suitable reagents for derivatizing alpha-amino-containing residues include imidoesters such as methyl picolinimidate; pyridoxal phosphate; pyridoxal; chloroborohydride; trinitrobenzenesulfonic acid; O-methylisourea; 2,4 pentanedione; and transaminase-catalyzed reaction with glyoxylate.

Arginyl residues may be modified by reaction with any one or combination of several conventional reagents, including phenylglyoxal, 2,3-butanedione, 1,2-cyclohexanedione, and ninhydrin. Derivatization of arginyl residues requires that the reaction be performed in alkaline conditions because of the high pKa of the guanidine functional group. Furthermore, these reagents may react with the groups of lysine as well as the arginine epsilon-amino group.

Specific modification of tyrosyl residues has been studied extensively, with particular interest in introducing spectral labels into tyrosyl residues by reaction with aromatic diazonium compounds or tetranitromethane. Most commonly, N-acetylimidazole and tetranitromethane are used to form O-acetyl tyrosyl species and 3-nitro derivatives, respectively.

Carboxyl sidechain groups (aspartyl or glutamyl) may be selectively modified by reaction with carbodiimides ($R'-N=C=N-R'$) such as 1-cyclohexyl-3-(2-morpholinyl-(4-ethyl) carbodiimide or 1-ethyl-3-(4-azonia-4,4-dimethylpentyl) carbodiimide. Furthermore, aspartyl and glutamyl residues may be converted to asparaginyl and glutaminyl residues by reaction with ammonium ions.

Glutaminyl and asparaginyl residues may be deamidated to the corresponding glutamyl and aspartyl residues. Alternatively, these residues are deamidated under mildly acidic conditions. Either form of these residues falls within the scope of this invention.

Cysteinyll residues can be replaced by amino acid residues or other moieties either to eliminate disulfide bonding or, conversely, to stabilize cross-linking. See, e.g., Bhatnagar *et al.* (1996), *J. Med. Chem.* 39: 3814-9.

Derivatization with bifunctional agents is useful for cross-linking the peptides or their functional derivatives to a water-insoluble support matrix or to other macromolecular vehicles. Commonly used cross-linking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), and bifunctional maleimides such as bis-N-maleimido-1,8-octane. Derivatizing agents such as methyl-3-[(p-azidophenyl)dithiol]propioimide yield photoactivatable intermediates that are capable of forming crosslinks in the presence of light. Alternatively, reactive water-insoluble matrices such as cyanogen bromide-activated carbohydrates

and the reactive substrates described in U.S. Pat. Nos. 3,969,287; 3,691,016; 4,195,128; 4,247,642; 4,229,537; and 4,330,440 are employed for protein immobilization.

Carbohydrate (oligosaccharide) groups may conveniently be
5 attached to sites that are known to be glycosylation sites in proteins. Generally, O-linked oligosaccharides are attached to serine (Ser) or threonine (Thr) residues while N-linked oligosaccharides are attached to asparagine (Asn) residues when they are part of the sequence Asn-X-Ser/Thr, where X can be any amino acid except proline. X is preferably
10 one of the 19 naturally occurring amino acids other than proline. The structures of N-linked and O-linked oligosaccharides and the sugar residues found in each type are different. One type of sugar that is commonly found on both is N-acetylneuraminic acid (referred to as sialic acid). Sialic acid is usually the terminal residue of both N-linked and O-
15 linked oligosaccharides and, by virtue of its negative charge, may confer acidic properties to the glycosylated compound. Such site(s) may be incorporated in the linker of the compounds of this invention and are preferably glycosylated by a cell during recombinant production of the polypeptide compounds (e.g., in mammalian cells such as CHO, BHK,
20 COS). However, such sites may further be glycosylated by synthetic or semi-synthetic procedures known in the art.

Other possible modifications include hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl or threonyl residues, oxidation of the sulfur atom in Cys, methylation of the alpha-amino
25 groups of lysine, arginine, and histidine side chains. Creighton, Proteins: Structure and Molecule Properties (W. H. Freeman & Co., San Francisco), pp. 79-86 (1983).

Compounds of the present invention may be changed at the DNA level, as well. The DNA sequence of any portion of the compound may be

changed to codons more compatible with the chosen host cell. For E. coli, which is the preferred host cell, optimized codons are known in the art. Codons may be substituted to eliminate restriction sites or to include silent restriction sites, which may aid in processing of the DNA in the selected host cell. The vehicle, linker and peptide DNA sequences may be modified to include any of the foregoing sequence changes.

Methods of Making

The compounds of this invention largely may be made in transformed host cells using recombinant DNA techniques. To do so, a recombinant DNA molecule coding for the peptide is prepared. Methods of preparing such DNA molecules are well known in the art. For instance, sequences coding for the peptides could be excised from DNA using suitable restriction enzymes. Alternatively, the DNA molecule could be synthesized using chemical synthesis techniques, such as the phosphoramidate method. Also, a combination of these techniques could be used.

The invention also includes a vector capable of expressing the peptides in an appropriate host. The vector comprises the DNA molecule that codes for the peptides operatively linked to appropriate expression control sequences. Methods of effecting this operative linking, either before or after the DNA molecule is inserted into the vector, are well known. Expression control sequences include promoters, activators, enhancers, operators, ribosomal binding sites, start signals, stop signals, cap signals, polyadenylation signals, and other signals involved with the control of transcription or translation.

The resulting vector having the DNA molecule thereon is used to transform an appropriate host. This transformation may be performed using methods well known in the art.

Any of a large number of available and well-known host cells may be used in the practice of this invention. The selection of a particular host is dependent upon a number of factors recognized by the art. These include, for example, compatibility with the chosen expression vector, toxicity of the peptides encoded by the DNA molecule, rate of transformation, ease of recovery of the peptides, expression characteristics, bio-safety and costs. A balance of these factors must be struck with the understanding that not all hosts may be equally effective for the expression of a particular DNA sequence. Within these general guidelines, useful microbial hosts include bacteria (such as E. coli sp.), yeast (such as Saccharomyces sp.) and other fungi, insects, plants, mammalian (including human) cells in culture, or other hosts known in the art.

Next, the transformed host is cultured and purified. Host cells may be cultured under conventional fermentation conditions so that the desired compounds are expressed. Such fermentation conditions are well known in the art. Finally, the peptides are purified from culture by methods well known in the art.

The compounds may also be made by synthetic methods. For example, solid phase synthesis techniques may be used. Suitable techniques are well known in the art, and include those described in Merrifield (1973), Chem. Polypeptides, pp. 335-61 (Katsoyannis and Panayotis eds.); Merrifield (1963), J. Am. Chem. Soc. 85: 2149; Davis et al. (1985), Biochem. Intl. 10: 394-414; Stewart and Young (1969), Solid Phase Peptide Synthesis; U.S. Pat. No. 3,941,763; Finn et al. (1976), The Proteins (3rd ed.) 2: 105-253; and Erickson et al. (1976), The Proteins (3rd ed.) 2: 257-527. Solid phase synthesis is the preferred technique of making individual peptides since it is the most cost-effective method of making small peptides.

Compounds that contain derivatized peptides or which contain non-peptide groups may be synthesized by well-known organic chemistry techniques.

Uses of the Compounds

In general. The compounds of this invention have pharmacologic activity resulting from their ability to bind to proteins of interest as agonists, mimetics or antagonists of the native ligands of such proteins of interest. The utility of specific compounds is shown in Table 2. The activity of these compounds can be measured by assays known in the art. For the TPO-mimetic and EPO-mimetic compounds, in vivo assays are further described in the Examples section herein.

In addition to therapeutic uses, the compounds of the present invention are useful in diagnosing diseases characterized by dysfunction of their associated protein of interest. In one embodiment, a method of detecting in a biological sample a protein of interest (e.g., a receptor) that is capable of being activated comprising the steps of: (a) contacting the sample with a compound of this invention; and (b) detecting activation of the protein of interest by the compound. The biological samples include tissue specimens, intact cells, or extracts thereof. The compounds of this invention may be used as part of a diagnostic kit to detect the presence of their associated proteins of interest in a biological sample. Such kits employ the compounds of the invention having an attached label to allow for detection. The compounds are useful for identifying normal or abnormal proteins of interest. For the EPO-mimetic compounds, for example, presence of abnormal protein of interest in a biological sample may be indicative of such disorders as Diamond Blackfan anemia, where it is believed that the EPO receptor is dysfunctional.

Therapeutic uses of EPO-mimetic compounds. The EPO-mimetic compounds of the invention are useful for treating disorders characterized by low red blood cell levels. Included in the invention are methods of modulating the endogenous activity of an EPO receptor in a mammal, preferably methods of increasing the activity of an EPO receptor. In

general, any condition treatable by erythropoietin, such as anemia, may also be treated by the EPO-mimetic compounds of the invention. These compounds are administered by an amount and route of delivery that is appropriate for the nature and severity of the condition being treated and
5 may be ascertained by one skilled in the art. Preferably, administration is by injection, either subcutaneous, intramuscular, or intravenous.

Therapeutic uses of TPO-mimetic compounds. For the TPO-mimetic compounds, one can utilize such standard assays as those described in WO95/26746 entitled "Compositions and Methods for
10 Stimulating Megakaryocyte Growth and Differentiation". In vivo assays also appear in the Examples hereinafter.

The conditions to be treated are generally those that involve an existing megakaryocyte/platelet deficiency or an expected megakaryocyte/platelet deficiency (e.g., because of planned surgery or
15 platelet donation). Such conditions will usually be the result of a deficiency (temporary or permanent) of active Mpl ligand in vivo. The generic term for platelet deficiency is thrombocytopenia, and hence the methods and compositions of the present invention are generally available for treating thrombocytopenia in patients in need thereof.

20 Thrombocytopenia (platelet deficiencies) may be present for various reasons, including chemotherapy and other therapy with a variety of drugs, radiation therapy, surgery, accidental blood loss, and other specific disease conditions. Exemplary specific disease conditions that involve thrombocytopenia and may be treated in accordance with this
25 invention are: aplastic anemia, idiopathic thrombocytopenia, metastatic tumors which result in thrombocytopenia, systemic lupus erythematosus, splenomegaly, Fanconi's syndrome, vitamin B12 deficiency; folic acid deficiency, May-Hegglin anomaly, Wiskott-Aldrich syndrome, and paroxysmal nocturnal hemoglobinuria. Also, certain treatments for AIDS

result in thrombocytopenia (e.g., AZT). Certain wound healing disorders might also benefit from an increase in platelet numbers.

With regard to anticipated platelet deficiencies, e.g., due to future surgery, a compound of the present invention could be administered
5 several days to several hours prior to the need for platelets. With regard to acute situations, e.g., accidental and massive blood loss, a compound of this invention could be administered along with blood or purified platelets.

The TPO-mimetic compounds of this invention may also be useful in
10 stimulating certain cell types other than megakaryocytes if such cells are found to express Mpl receptor. Conditions associated with such cells that express the Mpl receptor, which are responsive to stimulation by the Mpl ligand, are also within the scope of this invention.

The TPO-mimetic compounds of this invention may be used in any
15 situation in which production of platelets or platelet precursor cells is desired, or in which stimulation of the c-Mpl receptor is desired. Thus, for example, the compounds of this invention may be used to treat any condition in a mammal wherein there is a need of platelets, megakaryocytes, and the like. Such conditions are described in detail in the following exemplary sources:
20 WO95/26746; WO95/21919; WO95/18858; WO95/21920 and are incorporated herein.

The TPO-mimetic compounds of this invention may also be useful in maintaining the viability or storage life of platelets and/or megakaryocytes and related cells. Accordingly, it could be useful to include an effective amount of
25 one or more such compounds in a composition containing such cells.

The therapeutic methods, compositions and compounds of the present invention may also be employed, alone or in combination with other cytokines, soluble Mpl receptor, hematopoietic factors, interleukins, growth factors or antibodies in the treatment of disease states

characterized by other symptoms as well as platelet deficiencies. It is anticipated that the inventive compound will prove useful in treating some forms of thrombocytopenia in combination with general stimulators of hematopoiesis, such as IL-3 or GM-CSF. Other megakaryocytic stimulatory factors, i.e., meg-CSF, stem cell factor (SCF), leukemia inhibitory factor (LIF), oncostatin M (OSM), or other molecules with megakaryocyte stimulating activity may also be employed with Mpl ligand. Additional exemplary cytokines or hematopoietic factors for such co-administration include IL-1 alpha, IL-1 beta, IL-2, IL-3, IL-4, IL-5, IL-6, IL-11, colony stimulating factor-1 (CSF-1), SCF, GM-CSF, granulocyte colony stimulating factor (G-CSF), EPO, interferon-alpha (IFN-alpha), consensus interferon, IFN-beta, or IFN-gamma. It may further be useful to administer, either simultaneously or sequentially, an effective amount of a soluble mammalian Mpl receptor, which appears to have an effect of causing megakaryocytes to fragment into platelets once the megakaryocytes have reached mature form. Thus, administration of an inventive compound (to enhance the number of mature megakaryocytes) followed by administration of the soluble Mpl receptor (to inactivate the ligand and allow the mature megakaryocytes to produce platelets) is expected to be a particularly effective means of stimulating platelet production. The dosage recited above would be adjusted to compensate for such additional components in the therapeutic composition. Progress of the treated patient can be monitored by conventional methods.

In cases where the inventive compounds are added to compositions of platelets and/or megakaryocytes and related cells, the amount to be included will generally be ascertained experimentally by techniques and assays known in the art. An exemplary range of amounts is 0.1 µg—1 mg inventive compound per 10⁶ cells.

Pharmaceutical Compositions

In General. The present invention also provides methods of using pharmaceutical compositions of the inventive compounds. Such pharmaceutical compositions may be for administration for injection, or for oral, pulmonary, nasal, transdermal or other forms of administration. In general, the invention encompasses pharmaceutical compositions comprising effective amounts of a compound of the invention together with pharmaceutically acceptable diluents, preservatives, solubilizers, emulsifiers, adjuvants and/or carriers. Such compositions include diluents of various buffer content (*e.g.*, Tris-HCl, acetate, phosphate), pH and ionic strength; additives such as detergents and solubilizing agents (*e.g.*, Tween 80, Polysorbate 80), anti-oxidants (*e.g.*, ascorbic acid, sodium metabisulfite), preservatives (*e.g.*, Thimersol, benzyl alcohol) and bulking substances (*e.g.*, lactose, mannitol); incorporation of the material into particulate preparations of polymeric compounds such as polylactic acid, polyglycolic acid, etc. or into liposomes. Hyaluronic acid may also be used, and this may have the effect of promoting sustained duration in the circulation. Such compositions may influence the physical state, stability, rate of in vivo release, and rate of in vivo clearance of the present proteins and derivatives. See, *e.g.*, Remington's Pharmaceutical Sciences, 18th Ed. (1990, Mack Publishing Co., Easton, PA 18042) pages 1435-1712 which are herein incorporated by reference. The compositions may be prepared in liquid form, or may be in dried powder, such as lyophilized form. Implantable sustained release formulations are also contemplated, as are transdermal formulations.

Oral dosage forms. Contemplated for use herein are oral solid dosage forms, which are described generally in Chapter 89 of Remington's Pharmaceutical Sciences (1990), 18th Ed., Mack Publishing Co. Easton PA 18042, which is herein incorporated by reference. Solid dosage forms include tablets, capsules, pills, troches or lozenges, cachets or pellets. Also,

liposomal or proteinoid encapsulation may be used to formulate the present compositions (as, for example, proteinoid microspheres reported in U.S. Patent No. 4,925,673). Liposomal encapsulation may be used and the liposomes may be derivatized with various polymers (e.g., U.S. Patent
5 No. 5,013,556). A description of possible solid dosage forms for the therapeutic is given in Chapter 10 of Marshall, K., Modern Pharmaceutics (1979), edited by G. S. Banker and C. T. Rhodes, herein incorporated by reference. In general, the formulation will include the inventive compound, and inert ingredients which allow for protection against the
10 stomach environment, and release of the biologically active material in the intestine.

Also specifically contemplated are oral dosage forms of the above inventive compounds. If necessary, the compounds may be chemically modified so that oral delivery is efficacious. Generally, the chemical
15 modification contemplated is the attachment of at least one moiety to the compound molecule itself, where said moiety permits (a) inhibition of proteolysis; and (b) uptake into the blood stream from the stomach or intestine. Also desired is the increase in overall stability of the compound and increase in circulation time in the body. Moieties useful as covalently
20 attached vehicles in this invention may also be used for this purpose. Examples of such moieties include: PEG, copolymers of ethylene glycol and propylene glycol, carboxymethyl cellulose, dextran, polyvinyl alcohol, polyvinyl pyrrolidone and polyproline. See, for example, Abuchowski and Davis, Soluble Polymer-Enzyme Adducts, Enzymes as Drugs (1981),
25 Hocenberg and Roberts, eds., Wiley-Interscience, New York, NY, , pp 367-83; Newmark, et al. (1982), J. Appl. Biochem. 4:185-9. Other polymers that could be used are poly-1,3-dioxolane and poly-1,3,6-tioxocane. Preferred for pharmaceutical usage, as indicated above, are PEG moieties.

For oral delivery dosage forms, it is also possible to use a salt of a modified aliphatic amino acid, such as sodium N-(8-[2-hydroxybenzoyl] amino) caprylate (SNAC), as a carrier to enhance absorption of the therapeutic compounds of this invention. The clinical efficacy of a heparin
5 formulation using SNAC has been demonstrated in a Phase II trial conducted by Emisphere Technologies. See US Patent No. 5,792,451, "Oral drug delivery composition and methods".

The compounds of this invention can be included in the formulation as fine multiparticulates in the form of granules or pellets of
10 particle size about 1 mm. The formulation of the material for capsule administration could also be as a powder, lightly compressed plugs or even as tablets. The therapeutic could be prepared by compression.

Colorants and flavoring agents may all be included. For example, the protein (or derivative) may be formulated (such as by liposome or
15 microsphere encapsulation) and then further contained within an edible product, such as a refrigerated beverage containing colorants and flavoring agents.

One may dilute or increase the volume of the compound of the invention with an inert material. These diluents could include
20 carbohydrates, especially mannitol, α -lactose, anhydrous lactose, cellulose, sucrose, modified dextrans and starch. Certain inorganic salts may also be used as fillers including calcium triphosphate, magnesium carbonate and sodium chloride. Some commercially available diluents are Fast-Flo, Emdex, STA-Rx 1500, Emcompress and Avicell.

25 Disintegrants may be included in the formulation of the therapeutic into a solid dosage form. Materials used as disintegrants include but are not limited to starch including the commercial disintegrant based on starch, Explotab. Sodium starch glycolate, Amberlite, sodium carboxymethylcellulose, ultramylopectin, sodium alginate, gelatin, orange

peel, acid carboxymethyl cellulose, natural sponge and bentonite may all be used. Another form of the disintegrants are the insoluble cationic exchange resins. Powdered gums may be used as disintegrants and as binders and these can include powdered gums such as agar, Karaya or tragacanth. Alginic acid and its sodium salt are also useful as
5 disintegrants.

Binders may be used to hold the therapeutic agent together to form a hard tablet and include materials from natural products such as acacia, tragacanth, starch and gelatin. Others include methyl cellulose (MC), ethyl
10 cellulose (EC) and carboxymethyl cellulose (CMC). Polyvinyl pyrrolidone (PVP) and hydroxypropylmethyl cellulose (HPMC) could both be used in alcoholic solutions to granulate the therapeutic.

An antifrictional agent may be included in the formulation of the therapeutic to prevent sticking during the formulation process. Lubricants
15 may be used as a layer between the therapeutic and the die wall, and these can include but are not limited to; stearic acid including its magnesium and calcium salts, polytetrafluoroethylene (PTFE), liquid paraffin, vegetable oils and waxes. Soluble lubricants may also be used such as sodium lauryl sulfate, magnesium lauryl sulfate, polyethylene glycol of
20 various molecular weights, Carbowax 4000 and 6000.

Glidants that might improve the flow properties of the drug during formulation and to aid rearrangement during compression might be added. The glidants may include starch, talc, pyrogenic silica and hydrated silicoaluminate.

25 To aid dissolution of the compound of this invention into the aqueous environment a surfactant might be added as a wetting agent. Surfactants may include anionic detergents such as sodium lauryl sulfate, dioctyl sodium sulfosuccinate and dioctyl sodium sulfonate. Cationic detergents might be used and could include benzalkonium chloride or

benzethonium chloride. The list of potential nonionic detergents that could be included in the formulation as surfactants are lauromacrogol 400, polyoxyl 40 stearate, polyoxyethylene hydrogenated castor oil 10, 50 and 60, glycerol monostearate, polysorbate 40, 60, 65 and 80, sucrose fatty acid ester, methyl cellulose and carboxymethyl cellulose. These surfactants could be present in the formulation of the protein or derivative either alone or as a mixture in different ratios.

Additives may also be included in the formulation to enhance uptake of the compound. Additives potentially having this property are for instance the fatty acids oleic acid, linoleic acid and linolenic acid.

Controlled release formulation may be desirable. The compound of this invention could be incorporated into an inert matrix which permits release by either diffusion or leaching mechanisms e.g., gums. Slowly degenerating matrices may also be incorporated into the formulation, e.g., alginates, polysaccharides. Another form of a controlled release of the compounds of this invention is by a method based on the Oros therapeutic system (Alza Corp.), i.e., the drug is enclosed in a semipermeable membrane which allows water to enter and push drug out through a single small opening due to osmotic effects. Some enteric coatings also have a delayed release effect.

Other coatings may be used for the formulation. These include a variety of sugars which could be applied in a coating pan. The therapeutic agent could also be given in a film coated tablet and the materials used in this instance are divided into 2 groups. The first are the nonenteric materials and include methyl cellulose, ethyl cellulose, hydroxyethyl cellulose, methylhydroxy-ethyl cellulose, hydroxypropyl cellulose, hydroxypropyl-methyl cellulose, sodium carboxy-methyl cellulose, providone and the polyethylene glycols. The second group consists of the enteric materials that are commonly esters of phthalic acid.

A mix of materials might be used to provide the optimum film coating. Film coating may be carried out in a pan coater or in a fluidized bed or by compression coating.

Pulmonary delivery forms. Also contemplated herein is pulmonary
5 delivery of the present protein (or derivatives thereof). The protein (or
derivative) is delivered to the lungs of a mammal while inhaling and
traverses across the lung epithelial lining to the blood stream. (Other
reports of this include Adjei *et al.*, Pharma. Res. (1990) 7: 565-9; Adjei *et al.*
(1990), Internatl. J. Pharmaceutics 63: 135-44 (leuprolide acetate); Braquet
10 *et al.* (1989), J. Cardiovasc. Pharmacol. 13 (suppl.5): s.143-146 (endothelin-
1); Hubbard *et al.* (1989), Annals Int. Med. 3: 206-12 (α 1-antitrypsin); Smith
et al. (1989), J. Clin. Invest. 84: 1145-6 (α 1-proteinase); Oswein *et al.* (March
1990), "Aerosolization of Proteins", Proc. Symp. Resp. Drug Delivery II,
Keystone, Colorado (recombinant human growth hormone); Debs *et al.*
15 (1988), J. Immunol. 140: 3482-8 (interferon- γ and tumor necrosis factor α)
and Platz *et al.*, U.S. Patent No. 5,284,656 (granulocyte colony stimulating
factor).

Contemplated for use in the practice of this invention are a wide
range of mechanical devices designed for pulmonary delivery of
20 therapeutic products, including but not limited to nebulizers, metered
dose inhalers, and powder inhalers, all of which are familiar to those
skilled in the art. Some specific examples of commercially available
devices suitable for the practice of this invention are the Ultravent
nebulizer, manufactured by Mallinckrodt, Inc., St. Louis, Missouri; the
25 Acorn II nebulizer, manufactured by Marquest Medical Products,
Englewood, Colorado; the Ventolin metered dose inhaler, manufactured
by Glaxo Inc., Research Triangle Park, North Carolina; and the Spinhaler
powder inhaler, manufactured by Fisons Corp., Bedford, Massachusetts.

All such devices require the use of formulations suitable for the dispensing of the inventive compound. Typically, each formulation is specific to the type of device employed and may involve the use of an appropriate propellant material, in addition to diluents, adjuvants
5 and/or carriers useful in therapy.

The inventive compound should most advantageously be prepared in particulate form with an average particle size of less than 10 μm (or microns), most preferably 0.5 to 5 μm , for most effective delivery to the distal lung.

10 Pharmaceutically acceptable carriers include carbohydrates such as trehalose, mannitol, xylitol, sucrose, lactose, and sorbitol. Other ingredients for use in formulations may include DPPC, DOPE, DSPC and DOPC. Natural or synthetic surfactants may be used. PEG may be used (even apart from its use in derivatizing the protein or analog). Dextran,
15 such as cyclodextran, may be used. Bile salts and other related enhancers may be used. Cellulose and cellulose derivatives may be used. Amino acids may be used, such as use in a buffer formulation.

Also, the use of liposomes, microcapsules or microspheres, inclusion complexes, or other types of carriers is contemplated.

20 Formulations suitable for use with a nebulizer, either jet or ultrasonic, will typically comprise the inventive compound dissolved in water at a concentration of about 0.1 to 25 mg of biologically active protein per mL of solution. The formulation may also include a buffer and a simple sugar (e.g., for protein stabilization and regulation of osmotic
25 pressure). The nebulizer formulation may also contain a surfactant, to reduce or prevent surface induced aggregation of the protein caused by atomization of the solution in forming the aerosol.

Formulations for use with a metered-dose inhaler device will generally comprise a finely divided powder containing the inventive

compound suspended in a propellant with the aid of a surfactant. The propellant may be any conventional material employed for this purpose, such as a chlorofluorocarbon, a hydrochlorofluorocarbon, a hydrofluorocarbon, or a hydrocarbon, including trichlorofluoromethane, dichlorodifluoromethane, dichlorotetrafluoroethanol, and 1,1,1,2-tetrafluoroethane, or combinations thereof. Suitable surfactants include sorbitan trioleate and soya lecithin. Oleic acid may also be useful as a surfactant.

Formulations for dispensing from a powder inhaler device will comprise a finely divided dry powder containing the inventive compound and may also include a bulking agent, such as lactose, sorbitol, sucrose, mannitol, trehalose, or xylitol in amounts which facilitate dispersal of the powder from the device, e.g., 50 to 90% by weight of the formulation.

Nasal delivery forms. Nasal delivery of the inventive compound is also contemplated. Nasal delivery allows the passage of the protein to the blood stream directly after administering the therapeutic product to the nose, without the necessity for deposition of the product in the lung. Formulations for nasal delivery include those with dextran or cyclodextran. Delivery via transport across other mucous membranes is also contemplated.

Dosages. The dosage regimen involved in a method for treating the above-described conditions will be determined by the attending physician, considering various factors which modify the action of drugs, e.g. the age, condition, body weight, sex and diet of the patient, the severity of any infection, time of administration and other clinical factors. Generally, the daily regimen should be in the range of 0.1-1000 micrograms of the inventive compound per kilogram of body weight, preferably 0.1-150 micrograms per kilogram.

Specific preferred embodiments

- The inventors have determined preferred peptide sequences for molecules having many different kinds of activity. The inventors have further determined preferred structures of these preferred peptides combined with preferred linkers and vehicles. Preferred structures for these preferred peptides listed in Table 21 below.

Table 21—Preferred embodiments

| Sequence/structure | SEQ ID NO: | Activity |
|---|------------|-------------------------|
| F ¹ -(G) ₅ -IEGPTLRQWLAARA-(G) ₈ -IEGPTLRQWLAARA | 337 | TPO-mimetic |
| IEGPTLRQWLAARA-(G) ₈ -IEGPTLRQWLAARA-(G) ₅ -F ¹ | 338 | TPO-mimetic |
| F ¹ -(G) ₅ -IEGPTLRQWLAARA | 1032 | TPO-mimetic |
| IEGPTLRQWLAARA -(G) ₅ -F ¹ | 1033 | TPO-mimetic |
| F ¹ -(G) ₅ -GGTYSCHFGPLTWVCKPQGG-(G) ₄ -GGTYSCHFGPLTWVCKPQGG | 339 | EPO-mimetic |
| GGTYSCHFGPLTWVCKPQGG-(G) ₄ -GGTYSCHFGPLTWVCKPQGG-(G) ₅ -F ¹ | 340 | EPO-mimetic |
| GGTYSCHFGPLTWVCKPQGG-(G) ₅ -F ¹ | 1034 | EPO-mimetic |
| F ¹ -(G) ₅ -DFLPHYKNTSLGHRP | 1045 | TNF- α inhibitor |
| DFLPHYKNTSLGHRP-(G) ₅ -F ¹ | 1046 | TNF- α inhibitor |
| F ¹ -(G) ₅ -FEWTPGYWQPYALPL | 1047 | IL-1 R antagonist |
| FEWTPGYWQPYALPL-(G) ₅ -F ¹ | 1048 | IL-1 R antagonist |
| F ¹ -(G) ₅ -VEPNCDIHVMWEWECFERL | 1049 | VEGF-antagonist |
| VEPNCDIHVMWEWECFERL-(G) ₅ -F ¹ | 1050 | VEGF-antagonist |
| F ¹ -(G) ₅ -CTTHWGFTLC | 1051 | MMP inhibitor |
| CTTHWGFTLC-(G) ₅ -F ¹ | 1052 | MMP inhibitor |

"F¹" is an Fc domain as defined previously herein.

Working examples

The compounds described above may be prepared as described below. These examples comprise preferred embodiments of the invention and are illustrative rather than limiting.

Example 1

TPO-Mimetics

5

The following example uses peptides identified by the numbers appearing in Table A hereinafter.

Preparation of peptide 19. Peptide 17b (12 mg) and MeO-PEG-SH 5000 (30 mg, 2 equiv.) were dissolved in 1 ml aqueous buffer (pH 8). The mixture was incubated at RT for about 30 minutes and the reaction was checked by analytical HPLC, which showed a > 80% completion of the reaction. The pegylated material was isolated by preparative HPLC.

Preparation of peptide 20. Peptide 18 (14 mg) and MeO-PEG-maleimide (25 mg) were dissolved in about 1.5 ml aqueous buffer (pH 8). The mixture was incubated at RT for about 30 minutes, at which time about 70% transformation was complete as monitored with analytical HPLC by applying an aliquot of sample to the HPLC column. The pegylated material was purified by preparative HPLC.

Bioactivity assay. The TPO in vitro bioassay is a mitogenic assay utilizing an IL-3 dependent clone of murine 32D cells that have been transfected with human mpl receptor. This assay is described in greater detail in WO 95/26746. Cells are maintained in MEM medium containing 10% Fetal Clone II and 1 ng/ml mIL-3. Prior to sample addition, cells are prepared by rinsing twice with growth medium lacking mIL-3. An extended twelve point TPO standard curve is prepared, ranging from 33 to 39 pg/ml. Four dilutions, estimated to fall within the linear portion of the standard curve, (100 to 125 pg/ml), are prepared for each sample and run in triplicate. A volume of 100 µl of each dilution of sample or standard is added to appropriate wells of a 96 well microtiter plate

containing 10,000 cells/well. After forty-four hours at 37 °C and 10% CO₂, MTS (a tetrazolium compound which is bio-reduced by cells to a formazan) is added to each well. Approximately six hours later, the optical density is read on a plate reader at 490 nm. A dose response curve (log TPO

5 concentration vs. O.D.- Background) is generated and linear regression analysis of points which fall in the linear portion of the standard curve is performed. Concentrations of unknown test samples are determined using the resulting linear equation and a correction for the dilution factor.

TMP tandem repeats with polyglycine linkers. Our design of
10 sequentially linked TMP repeats was based on the assumption that a dimeric form of TMP was required for its effective interaction with c-Mpl (the TPO receptor) and that depending on how they were wound up against each other in the receptor context, the two TMP molecules could be tethered together in the C- to N-terminus configuration in a way that
15 would not perturb the global dimeric conformation. Clearly, the success of the design of tandem linked repeats depends on proper selection of the length and composition of the linker that joins the C- and N-termini of the two sequentially aligned TMP monomers. Since no structural information of the TMP bound to c-Mpl was available, a series of repeated peptides
20 with linkers composed of 0 to 10 and 14 glycine residues (Table A) were synthesized. Glycine was chosen because of its simplicity and flexibility, based on the rationale that a flexible polyglycine peptide chain might allow for the free folding of the two tethered TMP repeats into the required conformation, while other amino acid sequences may adopt
25 undesired secondary structures whose rigidity might disrupt the correct packing of the repeated peptide in the receptor context.

The resulting peptides are readily accessible by conventional solid phase peptide synthesis methods (Merrifield (1963), J. Amer. Chem. Soc. 85: 2149) with either Fmoc or t-Boc chemistry. Unlike the synthesis of the

C-terminally linked parallel dimer which required the use of an orthogonally protected lysine residue as the initial branch point to build the two peptide chains in a pseudosymmetrical way (Cwirla et al. (1997), Science 276: 1696-9), the synthesis of these tandem repeats was a straightforward, stepwise assembly of the continuous peptide chains from the C- to N-terminus. Since dimerization of TMP had a more dramatic effect on the proliferative activity than binding affinity as shown for the C-terminal dimer (Cwirla et al. (1997)), the synthetic peptides were tested directly for biological activity in a TPO-dependent cell-proliferation assay using an IL-3 dependent clone of murine 32D cells transfected with the full-length c-Mpl (Palacios et al., Cell 41:727 (1985)). As the test results showed, all the polyglycine linked tandem repeats demonstrated >1000 fold increases in potency as compared to the monomer, and were even more potent than the C-terminal dimer in this cell proliferation assay. The absolute activity of the C-terminal dimer in our assay was lower than that of the native TPO protein, which is different from the previously reported findings in which the C-terminal dimer was found to be as active as the natural ligand (Cwirla et al. (1997)). This might be due to differences in the conditions used in the two assays. Nevertheless, the difference in activity between tandem (C terminal of first monomer linked to N terminal of second monomer) and C-terminal (C terminal of first monomer linked to C terminal of second monomer; also referred to as parallel) dimers in the same assay clearly demonstrated the superiority of tandem repeat strategy over parallel peptide dimerization. It is interesting to note that a wide range of length is tolerated by the linker. The optimal linker between tandem peptides with the selected TMP monomers apparently is composed of 8 glycines.

Other tandem repeats. Subsequent to this first series of TMP tandem repeats, several other molecules were designed either with

different linkers or containing modifications within the monomer itself. The first of these molecules, peptide 13, has a linker composed of GPNG, a sequence known to have a high propensity to form a β -turn-type secondary structure. Although still about 100-fold more potent than the monomer, this peptide was found to be >10-fold less active than the equivalent GGGG-linked analog. Thus, introduction of a relatively rigid β -turn at the linker region seemed to have caused a slight distortion of the optimal agonist conformation in this short linker form.

The Trp9 in the TMP sequence is a highly conserved residue among the active peptides isolated from random peptide libraries. There is also a highly conserved Trp in the consensus sequences of EPO mimetic peptides and this Trp residue was found to be involved in the formation of a hydrophobic core between the two EMPs and contributed to hydrophobic interactions with the EPO receptor. Livnah *et al.* (1996), *Science* 273: 464-71). By analogy, the Trp9 residue in TMP might have a similar function in dimerization of the peptide ligand, and as an attempt to modulate and estimate the effects of noncovalent hydrophobic forces exerted by the two indole rings, several analogs were made resulting from mutations at the Trp. So in peptide 14, the Trp residue was replaced in each of the two TMP monomers with a Cys, and an intramolecular disulfide bond was formed between the two cysteines by oxidation which was envisioned to mimic the hydrophobic interactions between the two Trp residues in peptide dimerization. Peptide 15 is the reduced form of peptide 14. In peptide 16, the two Trp residues were replaced by Ala. As the assay data show, all three analogs were inactive. These data further demonstrated that Trp is critical for the activity of the TPO mimetic peptide, not just for dimer formation.

The next two peptides (peptide 17a, and 18) each contain in their 8-amino acid linker a Lys or Cys residue. These two compounds are

precursors to the two PEGylated peptides (peptide 19 and 20) in which the side chain of the Lys or Cys is modified by a PEG moiety. A PEG moiety was introduced at the middle of a relatively long linker, so that the large PEG component (5 kDa) is far enough away from the critical binding sites
5 in the peptide molecule. PEG is a known biocompatible polymer which is increasingly used as a covalent modifier to improve the pharmacokinetic profiles of peptide- and protein-based therapeutics.



A modular, solution-based method was devised for convenient PEGylation of synthetic or recombinant peptides. The method is based on
10 the now well established chemoselective ligation strategy which utilizes the specific reaction between a pair of mutually reactive functionalities. So, for pegylated peptide 19, the lysine side chain was preactivated with a bromoacetyl group to give peptide 17b to accommodate reaction with a thiol-derivatized PEG. To do that, an orthogonal protecting group, Dde,
15 was employed for the protection of the lysine ϵ -amine. Once the whole peptide chain was assembled, the N-terminal amine was reprotected with t-Boc. Dde was then removed to allow for the bromoacetylation. This strategy gave a high quality crude peptide which was easily purified using conventional reverse phase HPLC. Ligation of the peptide with the thiol-
20 modified PEG took place in aqueous buffer at pH 8 and the reaction completed within 30 minutes. MALDI-MS analysis of the purified, pegylated material revealed a characteristic, bell-shaped spectrum with an increment of 44 Da between the adjacent peaks. For PEG-peptide 20, a cysteine residue was placed in the linker region and its side chain thiol
25 group would serve as an attachment site for a maleimide-containing PEG. Similar conditions were used for the pegylation of this peptide. As the assay data revealed, these two pegylated peptides had even higher in vitro bioactivity as compared to their unpegylated counterparts.

Peptide 21 has in its 8-amino acid linker a potential glycosylation motif, NGS. Since our exemplary tandem repeats are made up of natural amino acids linked by peptide bonds, expression of such a molecule in an appropriate eukaryotic cell system should produce a glycopeptide with the carbohydrate moiety added on the side chain carboxamide of Asn. Glycosylation is a common post-translational modification process which can have many positive impacts on the biological activity of a given protein by increasing its aqueous solubility and in vivo stability. As the assay data show, incorporation of this glycosylation motif into the linker maintained high bioactivity. The synthetic precursor of the potential glycopeptide had in effect an activity comparable to that of the $-(G)_8$ -linked analog. Once glycosylated, this peptide is expected to have the same order of activity as the pegylated peptides, because of the similar chemophysical properties exhibited by a PEG and a carbohydrate moiety.

The last peptide is a dimer of a tandem repeat. It was prepared by oxidizing peptide 18, which formed an intermolecular disulfide bond between the two cysteine residues located at the linker. This peptide was designed to address the possibility that TMP was active as a tetramer. The assay data showed that this peptide was not more active than an average tandem repeat on an adjusted molar basis, which indirectly supports the idea that the active form of TMP is indeed a dimer, otherwise dimerization of a tandem repeat would have a further impact on the bioactivity.

In order to confirm the in vitro data in animals, one pegylated TMP tandem repeat (compound 20 in Table A) was delivered subcutaneously to normal mice via osmotic pumps. Time and dose-dependent increases were seen in platelet numbers for the duration of treatment. Peak platelet levels over 4-fold baseline were seen on day 8. A dose of $10\text{ }\mu\text{g/kg/day}$ of the pegylated TMP repeat produced a similar response to rHuMGDF (non-pegylated) at $100\text{ }\mu\text{g/kg/day}$ delivered by the same route.

Table A—TPO-mimetic Peptides

| Peptide No. | Compound | SEQ ID NO: | Relative Potency |
|----------------------------|---|---------------|---------------------|
| | TPO | | ++++ |
| | TMP monomer | 13 | + |
| | TMP C-C dimer | | +++- |
| TMP-(G) _n -TMP: | | | |
| 1 | n = 0 | 341 | ++++- |
| 2 | n = 1 | 342 | ++++ |
| 3 | n = 2 | 343 | ++++ |
| 4 | n = 3 | 344 | ++++ |
| 5 | n = 4 | 345 | ++++ |
| 6 | n = 5 | 346 | ++++ |
| 7 | n = 6 | 347 | ++++ |
| 8 | n = 7 | 348 | ++++ |
| 9 | n = 8 | 349 | ++++- |
| 10 | n = 9 | 350 | ++++ |
| 11 | n = 10 | 351 | ++++ |
| 12 | n = 14 | 352 | ++++ |
| 13 | TMP-GPNG-TMP | 353 | +++ |
| 14 | IEGPTLRQCLAARA-GGGGGGGG-IEGPTLRQCLAARA  | 354 | - |
| 15 | (cyclic) IEGPTLRQCLAARA-GGGGGGGG- IEGPTLRQCLAARA (linear) | 355 | - |
| 16 | IEGPTLRQALAARA-GGGGGGGG- IEGPTLRQALAARA | 356 | - |
| 17a | TMP-GGGKGGGG-TMP | 357 | ++++ |
| 17b | TMP-GGGK(BrAc)GGGG-TMP | 358 | ND |
| 18 | TMP-GGGCGGGG-TMP | 359 | ++++ |
| 19 | TMP-GGGK(PEG)GGGG-TMP | 360 | +++++ |
| 20 | TMP-GGGC(PEG)GGGG-TMP | 361 | +++++ |
| 21 | TMP-GGGN*GSGG-TMP | 362 | ++++ |
| 22 | TMP-GGGCGGGG-TMP  | 363 | ++++ |
| | TMP-GGGCGGGG-TMP | 363 | |

Discussion. It is well accepted that MGDF acts in a way similar to hGH, i.e., one molecule of the protein ligand binds two molecules of the receptor for its activation. Wells *et al.* (1996), *Ann. Rev. Biochem.* 65: 609-34. Now, this interaction is mimicked by the action of a much smaller peptide, TMP. However, the present studies suggest that this mimicry requires the concerted action of two TMP molecules, as covalent dimerization of TMP in either a C-C parallel or C-N sequential fashion increased the *in vitro* biological potency of the original monomer by a factor of greater than 10^3 . The relatively low biopotency of the monomer is probably due to inefficient formation of the noncovalent dimer. A preformed covalent repeat has the ability to eliminate the entropy barrier for the formation of a noncovalent dimer which is exclusively driven by weak, noncovalent interactions between two molecules of the small, 14-residue peptide.

It is intriguing that this tandem repeat approach had a similar effect on enhancing bioactivity as the reported C-C dimerization is intriguing. These two strategies brought about two very different molecular configurations. The C-C dimer is a quasi-symmetrical molecule, while the tandem repeats have no such symmetry in their linear structures. Despite this difference in their primary structures, these two types of molecules appeared able to fold effectively into a similar biologically active conformation and cause the dimerization and activation of c-Mpl. These experimental observations provide a number of insights into how the two TMP molecules may interact with one another in binding to c-Mpl. First, the two C-termini of the two bound TMP molecules must be in relatively close proximity with each other, as suggested by data on the C-terminal dimer. Second, the respective N- and C-termini of the two TMP molecules in the receptor complex must also be very closely aligned with each other, such that they can be directly tethered together with a single peptide bond

to realize the near maximum activity-enhancing effect brought about by the tandem repeat strategy. Insertion of one or more (up to 14) glycine residues at the junction did not increase (or decrease) significantly the activity any further. This may be due to the fact that a flexible polyglycine peptide chain is able to loop out easily from the junction without causing any significant changes in the overall conformation. This flexibility seems to provide the freedom of orientation for the TMP peptide chains to fold into the required conformation in interacting with the receptor and validate it as a site of modification. Indirect evidence supporting this came from the study on peptide 13, in which a much more rigid b-turn-forming sequence as the linker apparently forced a deviation of the backbone alignment around the linker which might have resulted in a slight distortion of the optimal conformation, thus resulting in a moderate (10-fold) decrease in activity as compared with the analogous compound with a 4-Gly linker. Third, Trp9 in TMP plays a similar role as Trp13 in EMP, which is involved not only in peptide:peptide interaction for the formation of dimers but also is important for contributing hydrophobic forces in peptide:receptor interaction. Results obtained with the W to C mutant analog, peptide 14, suggest that a covalent disulfide linkage is not sufficient to approximate the hydrophobic interactions provided by the Trp pair and that, being a short linkage, it might bring the two TMP monomers too close, therefore perturbing the overall conformation of the optimal dimeric structure.

An analysis of the possible secondary structure of the TMP peptide can provide further understanding on the interaction between TMP and c-Mpl. This can be facilitated by making reference to the reported structure of the EPO mimetic peptide. Livnah *et al.* (1996), *Science* 273:464-75 The receptor-bound EMP has a b-hairpin structure with a b-turn formed by the highly consensus Gly-Pro-Leu-Thr at the center of its sequence. Instead of

GPLT, TMP has a highly selected GPTL sequence which is likely to form a similar turn. However, this turn-like motif is located near the N-terminal part in TMP. Secondary structure prediction using Chau-Fasman method suggests that the C-terminal half of the peptide has a tendency to adopt a helical conformation. Together with the highly conserved Trp at position 9, this C-terminal helix may contribute to the stabilization of the dimeric structure. It is interesting to note that most of our tandem repeats are more potent than the C-terminal parallel dimer. Tandem repeats seem to give the molecule a better fit conformation than does the C-C parallel dimerization. The seemingly asymmetric feature of a tandem repeat might have brought it closer to the natural ligand which, as an asymmetric molecule, uses two different sites to bind two identical receptor molecules.

Introduction of a PEG moiety was envisaged to enhance the in vivo activity of the modified peptide by providing it a protection against proteolytic degradation and by slowing down its clearance through renal filtration. It was unexpected that pegylation could further increase the in vitro bioactivity of a tandem repeated TMP peptide in the cell-based proliferation assay.

Example 2

Fc-TMP fusions

TMPs (and EMPs as described in Example 3) were expressed in either monomeric or dimeric form as either N-terminal or C-terminal fusions to the Fc region of human IgG1. In all cases, the expression construct utilized the luxPR promoter promoter in the plasmid expression vector pAMG21.

Fc-TMP. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a monomer of the TPO-mimetic peptide was constructed using standard PCR technology. Templates for PCR reactions were the pFc-A3 vector and a synthetic TMP gene. The synthetic gene was

constructed from the 3 overlapping oligonucleotides (SEQ ID NOS: 364, 365, and 366, respectively) shown below:

```

1842-97      AAA AAA GGA TCC TCG AGA TTA AGC ACG AGC AGC CAG CCA
              CTG ACG CAG AGT CGG ACC
5
1842-98      AAA GGT GGA GGT GGT GGT ATC GAA GGT CCG ACT CTG CGT
1842-99      CAG TGG CTG GCT GCT CGT GCT TAA TCT CGA GGA TCC TTT
              TTT
10

```

These oligonucleotides were annealed to form the duplex encoding an amino acid sequence (SEQ ID NOS: 367 and 368, respectively) shown below:

```

15      AAAGGTGGAGGTGGTGGTATCGAAGGTCCGACTCTGCGTCAGTGGCTGGCTGCTCGTGCT
        1  -----+-----+-----+-----+-----+-----+-----+-----+ 60
a      K G G G G G I E G P T L R Q W L A A R A -
20      TAATCTCGAGGATCCTTTTTT
        61 -----+-----+-----+-----+-----+-----+-----+-----+ 81
a      ATTAGAGCTCCTAGGAAAAAA
        *

```

25 This duplex was amplified in a PCR reaction using 1842-98 and 1842-97 as the sense and antisense primers.

The Fc portion of the molecule was generated in a PCR reaction with pFc-A3 using the primers shown below (SEQ ID NOS: 369 and 370):

```

30 1216-52      AAC ATA AGT ACC TGT AGG ATC G
    1830-51      TTCGATACCA CCACCTCCAC CTTTACCCGG AGACAGGGAG AGGCTCTTCTGC

```

35 The oligonucleotides 1830-51 and 1842-98 contain an overlap of 24 nucleotides, allowing the two genes to be fused together in the correct reading frame by combining the above PCR products in a third reaction using the outside primers, 1216-52 and 1842-97.

40 The final PCR gene product (the full length fusion gene) was digested with restriction endonucleases XbaI and BamHI, and then ligated into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described for EMP-Fc herein. Clones were screened for the ability to produce the recombinant protein product and to possess the

gene fusion having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #3728.

The nucleotide and amino acid sequences (SEQ ID NOS: 5 and 6) of the fusion protein are shown in Figure 7.

5 Fc-TMP-TMP. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a dimer of the TPO-mimetic peptide was constructed using standard PCR technology. Templates for PCR reactions were the pFc-A3 vector and a synthetic TMP-TMP gene. The synthetic gene was constructed from the 4 overlapping oligonucleotides (SEQ ID
10 NOS: 371 to 374, respectively) shown below:

```

1830-52      AAA GGT GGA GGT GGT GGT ATC GAA GGT CCG
              ACT CTG CGT CAG TGG CTG GCT GCT CGT GCT
15  1830-53      ACC TCC ACC ACC AGC ACG AGC AGC CAG
              CCA CTG ACG CAG AGT CGG ACC
1830-54      GGT GGT GGA GGT GGC GGC GGA GGT ATT GAG GGC CCA ACC
              CTT CGC CAA TGG CTT GCA GCA CGC GCA
20  1830-55      AAA AAA AGG ATC CTC GAG ATT ATG CGC GTG CTG CAA GCC
              ATT GGC GAA GGG TTG GGC CCT CAA TAC CTC CGC CGC C

```

25 The 4 oligonucleotides were annealed to form the duplex encoding an amino acid sequence (SEQ ID NOS: 375 and 376, respectively) shown below:

```

30  1      AAAGGTGGAGGTGGTGGTATCGAAGGTCCGACTCTGCGTCAGTGGCTGGCTGCTCGTGCT
      1 -----+-----+-----+-----+-----+-----+-----+-----+ 60
      a      K G G G G G I E G P T L R Q W L A A R A -
              CCAGGCTGAGACGCAGTCACCGACCGACGAGCACGA
35  61      GGTGGTGGAGGTGGCGGCGGAGGTATTGAGGGCCCAACCCTTCGCCAATGGCTTGCAGCA
      61 -----+-----+-----+-----+-----+-----+-----+ 120
      a      G G G G G G G G I E G P T L R Q W L A A -
              CGCGCA
40  121     GCGCGTATTAGAGCTCCTAGGAAAAAA
      121 -----+-----+-----+-----+-----+-----+-----+ 148
      a      R A * -

```

45 This duplex was amplified in a PCR reaction using 1830-52 and 1830-55 as the sense and antisense primers.

The Fc portion of the molecule was generated in a PCR reaction with pFc-A3 using the primers 1216-52 and 1830-51 as described above for

Fc-TMP. The full length fusion gene was obtained from a third PCR reaction using the outside primers 1216-52 and 1830-55.

The final PCR gene product (the full length fusion gene) was digested with restriction endonucleases XbaI and BamHI, and then ligated into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described in example 1. Clones were screened for the ability to produce the recombinant protein product and to possess the gene fusion having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #3727.

The nucleotide and amino acid sequences (SEQ ID NOS: 7 and 8) of the fusion protein are shown in Figure 8.

TMP-TMP-Fc. A DNA sequence coding for a tandem repeat of the TPO-mimetic peptide fused in-frame to the Fc region of human IgG1 was constructed using standard PCR technology. Templates for PCR reactions were the EMP-Fc plasmid from strain #3688 (see Example 3) and a synthetic gene encoding the TMP dimer. The synthetic gene for the tandem repeat was constructed from the 7 overlapping oligonucleotides shown below (SEQ ID NOS: 377 to 383, respectively):

| | | |
|----|---------|--|
| 20 | 1885-52 | TTT TTT CAT ATG ATC GAA GGT CCG ACT CTG CGT CAG TGG |
| | 1885-53 | AGC ACG AGC AGC CAG CCA CTG ACG CAG AGT CGG ACC TTC GAT CAT ATG |
| 25 | 1885-54 | CTG GCT GCT CGT GCT GGT GGA GGC GGT GGG GAC AAA ACT CAC ACA |
| | 1885-55 | CTG GCT GCT CGT GCT GGC GGT GGT GGC GGA GGG GGT GGC ATT GAG GGC CCA |
| 30 | 1885-56 | AAG CCA TTG GCG AAG GGT TGG GCC CTC AAT GCC ACC CCC TCC GCC ACC ACC GCC |
| | 1885-57 | ACC CTT CGC CAA TGG CTT GCA GCA CGC GCA GGG GGA GGC GGT GGG GAC AAA ACT |
| 35 | 1885-58 | CCC ACC GCC TCC CCC TGC GCG TGC TGC |

These oligonucleotides were annealed to form the duplex shown encoding an amino acid sequence shown below (SEQ ID NOS 384 and 385):

```

      TTTTTCATATGATCGAAGGTCCGACTCTGCGTCAGTGGCTGGCTGCTCGTGCTGGCGGT
1  -----+-----+-----+-----+-----+-----+-----+-----+ 60
      GTATACTAGCTTCCAGGCTGAGACGCAGTCACCGACCGACGAGCACGACCGCCA
a      M I E G P T L R Q W L A A R A G G -
5
      GGTGGCGGAGGGGGTGGCATTGAGGGCCCAACCCTTCGCCAATGGCTGGCTGCTCGTGCT
61 -----+-----+-----+-----+-----+-----+-----+ 120
      CCACCGCTCCCCACCGTAACGCCGGTTGGGAAGCGGTTACCGAACGTCGTGCGCGT
a      G G G G G I E G P T L R Q W L A A R A -
10
      GGTGGAGGCGGTGGGGACAAAACCTCTGGCTGCTCGTGCTGGTGGAGGCGGTGGGGACAAA
121 -----+-----+-----+-----+-----+-----+-----+ 180
      CCCCCCTCCGCCACCC
a      G G G G G D K T L A A R A G G G G G D K -
15
      ACTCACACA
181 ----- 189
a      T H T -
20

```

This duplex was amplified in a PCR reaction using 1885-52 and 1885-58 as the sense and antisense primers.

The Fc portion of the molecule was generated in a PCR reaction with DNA from the EMP-Fc fusion strain #3688 (see Example 3) using the primers 1885-54 and 1200-54. The full length fusion gene was obtained from a third PCR reaction using the outside primers 1885-52 and 1200-54.

The final PCR gene product (the full length fusion gene) was digested with restriction endonucleases XbaI and BamHI, and then ligated into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described for Fc-EMP herein. Clones were screened for the ability to produce the recombinant protein product and to possess the gene fusion having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #3798.

The nucleotide and amino acid sequences (SEQ ID NOS: 9 and 10) of the fusion protein are shown in Figure 9.

TMP-Fc. A DNA sequence coding for a monomer of the TPO-mimetic peptide fused in-frame to the Fc region of human IgG1 was obtained fortuitously in the ligation in TMP-TMP-Fc, presumably due to the ability of primer 1885-54 to anneal to 1885-53 as well as to 1885-58. A single clone having the correct nucleotide sequence for the TMP-Fc construct was selected and designated Amgen strain #3788.

The nucleotide and amino acid sequences (SEQ ID NOS: 11 and 12) of the fusion protein are shown in Figure 10.

Expression in E. coli. Cultures of each of the pAMG21-Fc-fusion constructs in E. coli GM221 were grown at 37 °C in Luria Broth medium containing 50 mg/ml kanamycin. Induction of gene product expression from the luxPR promoter was achieved following the addition of the synthetic autoinducer N-(3-oxohexanoyl)-DL-homoserine lactone to the culture media to a final concentration of 20 ng/ml. Cultures were incubated at 37 °C for a further 3 hours. After 3 hours, the bacterial cultures were examined by microscopy for the presence of inclusion bodies and were then collected by centrifugation. Refractile inclusion bodies were observed in induced cultures indicating that the Fc-fusions were most likely produced in the insoluble fraction in E. coli. Cell pellets were lysed directly by resuspension in Laemmli sample buffer containing 10% b-mercaptoethanol and were analyzed by SDS-PAGE. In each case, an intense coomassie-stained band of the appropriate molecular weight was observed on an SDS-PAGE gel.

pAMG21. The expression plasmid pAMG21 can be derived from the Amgen expression vector pCFM1656 (ATCC #69576) which in turn be derived from the Amgen expression vector system described in US Patent No. 4,710,473. The pCFM1656 plasmid can be derived from the described pCFM836 plasmid (Patent No. 4,710,473) by:

- (a) destroying the two endogenous NdeI restriction sites by end filling with T4 polymerase enzyme followed by blunt end ligation;
- (b) replacing the DNA sequence between the unique AatII and ClaI restriction sites containing the synthetic P_L promoter with a similar fragment obtained from pCFM636 (patent No. 4,710,473) containing the PL promoter (see SEQ ID NO: 386 below); and

(c) substituting the small DNA sequence between the unique Clal and KpnI restriction sites with the oligonucleotide having the sequence of SEQ ID NO: 388.

SEQ ID NO: 386:

5 AatII
 5' CTAATTCCGCTCTCACCTACCAAACAATGCCCCCTGCAAAAAATAAATTCATAT-
 3' TGCAGATTAAGGCGAGAGTGGATGGTTTGTTACGGGGGACGTTTTTTATTTAAGTATA-

 10 -AAAAAACATACAGATAACCATCTGCCGTGATAAAATTATCTCTGCCGGTGTTGACATAAAA-
 -TTTTTTGTATGCTATTGGTAGACGCCACTATTTAATAGAGACCGCCACAACGTGATTT-

 -TACCACTGGCGGTGATACTGAGCAT 3'
 -ATGGTGACCGCCACTATGACTCGTGTAGC 5'

ClaI

SEQ ID NO: 387:

5' CGATTTGATTCTAGAAGGAGGAATAACATATGGTTAACGCGTTGGAATTCGGTAC 3'
3' TAACTAAGATCTTCTCCTTATTGTATACCAATTGCGCAACCTTAAGC 5'

ClaI **KpnI**

20 The expression plasmid pAMG21 can then be derived from pCFM1656 by making a series of site-directed base changes by PCR overlapping oligo mutagenesis and DNA sequence substitutions. Starting with the BglIII site (plasmid bp # 180) immediately 5' to the plasmid replication promoter

25 P_{copB} and proceeding toward the plasmid replication genes, the base pair changes are as shown in Table B below.

Table B—Base pair changes resulting in pAMG21

| | <u>pAMG21 bp #</u> | <u>bp in pCFM1656</u> | <u>bp changed to in pAMG21</u> |
|----|--------------------|---------------------------|--------------------------------|
| 5 | # 204 | T/A | C/G |
| | # 428 | A/T | G/C |
| | # 509 | G/C | A/T |
| | # 617 | -- | insert two G/C bp |
| | # 679 | G/C | T/A |
| 10 | # 980 | T/A | C/G |
| | # 994 | G/C | A/T |
| | # 1004 | A/T | C/G |
| | # 1007 | C/G | T/A |
| | # 1028 | A/T | T/A |
| 15 | # 1047 | C/G | T/A |
| | # 1178 | G/C | T/A |
| | # 1466 | G/C | T/A |
| | # 2028 | G/C | bp deletion |
| | # 2187 | C/G | T/A |
| 20 | # 2480 | A/T | T/A |
| | # 2499-2502 | <u>AGTG</u> TCAC | <u>GTCA</u> CAGT |
| 25 | # 2642 | <u>TCCGAGC</u> AGGCTCG | 7 bp deletion |
| | # 3435 | G/C | A/T |
| 30 | # 3446 | G/C | A/T |
| | # 3643 | A/T | T/A |

The DNA sequence between the unique AatII (position #4364 in pCFM1656) and SacII (position #4585 in pCFM1656) restriction sites is substituted with the DNA sequence (SEQ ID NO: 23) shown in Figures 17A and 17B. During the ligation of the sticky ends of this substitution DNA sequence, the outside AatII and SacII sites are destroyed. There are unique AatII and SacII sites in the substituted DNA.

GM221 (Amgen #2596). The Amgen host strain #2596 is an E.coli K-12 strain derived from Amgen strain #393. It has been modified to contain both the temperature sensitive lambda repressor cI857s7 in the early ebg region and the lacI^Q repressor in the late ebg region (68 minutes). The presence of these two repressor genes allows the use of this host with a variety of expression systems, however both of these repressors are irrelevant to the expression from luxP_R. The untransformed host has no antibiotic resistances.

The ribosome binding site of the cI857s7 gene has been modified to include an enhanced RBS. It has been inserted into the ebg operon between nucleotide position 1170 and 1411 as numbered in Genbank accession number M64441Gb_Ba with deletion of the intervening ebg sequence. The sequence of the insert is shown below with lower case letters representing the ebg sequences flanking the insert shown below (SEQ ID NO: 388):

```

ttatttttcgtGCGGCCGCACCATTTATCACCGCCAGAGGTAAACTAGTCAACACGCACGGTGTAGATATTTAT
CCCTTGCGGTGATAGATTGAGCACATCGATTTGATCTAGAAGGAGGGATAATATATGAGCACAAAAAGAAA
25 CCATTAACACAAGAGCAGCTTGAGGACGCACGTCGCCTTAAAGCAATTTATGAAAAAAGAAAAATGAACCTG
GCTTATCCCAGGAATCTGTGCGCAGACAAGATGGGGATGGGGCAGTCAGGCGTTGGTGCTTTATTTAATGGCAT
CAATGCATTAAATGCTTATAACGCCGATTGCTTACAAAAATTCTCAAAGTTAGCGTTGAAGAATTTAGCCCT
TCAATCGCCAGAGAATCTACGAGATGTATGAAGCGTTAGTATGCAGCCGTCACCTAGAAAGTGAGTATGAGTA
CCCTGTTTTTTCTCATGTTTCAGGCAGGGATGTTCTCACCTAAGCTTAGAACCTTTACCAAAGGTGATGCGGAG
AGATGGGTAAGCACAACCAAAAAAGCCAGTGAATCTGCATTCTGGCTTGAGGTTGAAGGTAATTCATGACCG
30 CACCAACAGGCTCCAAGCCAAGCTTTTCCTGACGGAATGTTAATTCTCGTTGACCCTGAGCAGGCTGTTGAGCC
AGGTGATTTCTGCATAGCCAGACTTGGGGGTGATGAGTTTACCTTCAAGAACTGATCAGGGATAGCGGTCAG
GTGTTTTTACAACCACTAAACCCACAGTACCCAATGATCCCATGCAATGAGAGTTGTTCCGTTGTGGGGAAG
TTATCGCTAGTCAGTGGCCTGAAGAGACGTTTGGCTGATAGACTAGTGGATCCACTAGTgtttctgccc

```

The construct was delivered to the chromosome using a recombinant phage called MMEbg-cI857s7enhanced RBS #4 into F'tet/393. After recombination and resolution only the chromosomal insert described

above remains in the cell. It was renamed F'tet/GM101. F'tet/GM101 was then modified by the delivery of a lacI^Q construct into the ebg operon between nucleotide position 2493 and 2937 as numbered in the Genbank accession number M64441Gb_Ba with the deletion of the intervening ebg sequence. The sequence of the insert is shown below with the lower case letters representing the ebg sequences flanking the insert (SEQ ID NO: 389) shown below:

```

10  ggcggaaaccgacgtccatcgaatgggtgcaaaccttttcgCGGTATGGCATGATAGCGCCCGGAAGAGAGTCA
    ATTCAGGGTGGTGAATGTGAAACCAGTAACGTTATACGATGTCGCAGAGTATGCCGGTGTCTCTTATCAGACC
    GTTTCCTCGCGTGGTGAACCAGGCCAGCCACGTTTCTGCGAAAACGCGGGAAAAAGTCGAAGCGGCGATGGCGG
    AGCTGAATTACATTCCCAACCGCGTGGCACAACAACCTGGCGGGCAAAACAGTCGCTCCTGATTGGCGTTGCCAC
    CTCCAGTCTGGCCCTGCACGCGCCGTCGCAAAATTGTCGCGCGGATTAAATCTCGCGCCGATCAACTGGGTGCC
    AGCGTGGTGGTGTGCGATGGTAGAACGAAGCGGCGTCGAAGCCTGTAAAGCGGCGGTGCACAATCTTCTCGCGC
    AACCGCTCAGTGGGCTGATCATTAACTATCCGCTGGATGACCAGGATGCCATTGCTGTGGAAGCTGCCTGCAC
15  TAATGTTCCGGCGTTATTTCTTGATGTCTCTGACCAGACACCCATCAACAGTATTATTTTCTCCCATGAAGAC
    GGTACGCGACTGGGCGTGGAGCATCTGGTCGCATTGGGTACCAGCAAATCGCGCTGTTAGCGGGCCATTAA
    GTTCTGTCTCGGCGCTCTGCGTCTGGCTGGCTGGCATAAATATCTCACTCGCAATCAAATTCAGCCGATAGC
    GGAACGGGAAGGCGACTGGAGTGCCATGTCCGGTTTTTCAACAAACCATGCAAAATGCTGAATGAGGGCATCGTT
20  CCCACTGCGATGCTGGTTGCCAACGATCAGATGGCGCTGGGCGCAATGCGCGCCATTACCGAGTCCGGGCTGC
    GCGTTGGTGGGATATCTCGGTAGTGGGATACGACGATACCGAAGACAGCTCATGTTATATCCCGCCGTTAAC
    CACCATCAAACAGGATTTTCGCCTGCTGGGGCAAACAGCGTGGACCGCTTGCTGCAACTCTCTCAGGGCCAG
    GCGGTGAAGGGCAATCAGCTGTTGCCCCGTCTCACTGGTGAAAAGAAAAACCACCTGGCGCCCAATACGCAAA
    CCGCCTCTCCCCGCGGTTGGCCGATTCATTAATGCAGCTGGCACGACAGGTTTCCCGACTGGAAAGCGGACA
25  GTAAGGTACCATAGGATCCaggcacagga

```

The construct was delivered to the chromosome using a recombinant phage called AGebg-LacIQ#5 into F'tet/GM101. After recombination and resolution only the chromosomal insert described above remains in the cell. It was renamed F'tet/GM221. The F'tet episome was cured from the strain using acridine orange at a concentration of 25 µg/ml in LB. The cured strain was identified as tetracycline sensitive and was stored as GM221.

Expression. Cultures of pAMG21-Fc-TMP-TMP in *E. coli* GM221 in Luria Broth medium containing 50 µg/ml kanamycin were incubated at 37°C prior to induction. Induction of Fc-TMP-TMP gene product expression from the luxPR promoter was achieved following the addition of the synthetic autoinducer N-(3-oxohexanoyl)-DL-homoserine lactone to the culture media to a final concentration of 20 ng/ml and cultures were incubated at 37°C for a further 3 hours. After 3 hours, the bacterial

cultures were examined by microscopy for the presence of inclusion bodies and were then collected by centrifugation. Refractile inclusion bodies were observed in induced cultures indicating that the Fc-TMP-TMP was most likely produced in the insoluble fraction in *E. coli*. Cell pellets
5 were lysed directly by resuspension in Laemmli sample buffer containing 10% β -mercaptoethanol and were analyzed by SDS-PAGE. An intense Coomassie stained band of approximately 30kDa was observed on an SDS-PAGE gel. The expected gene product would be 269 amino acids in length and have an expected molecular weight of about 29.5 kDa.

10 Fermentation was also carried out under standard batch conditions at the 10 L scale, resulting in similar expression levels of the Fc-TMP-TMP to those obtained at bench scale.

Purification of Fc-TMP-TMP. Cells are broken in water (1/10) by high pressure homogenization (2 passes at 14,000 PSI) and inclusion
15 bodies are harvested by centrifugation (4200 RPM in J-6B for 1 hour). Inclusion bodies are solubilized in 6M guanidine, 50mM Tris, 8mM DTT, pH 8.7 for 1 hour at a 1/10 ratio. The solubilized mixture is diluted 20 times into 2M urea, 50 mM tris, 160mM arginine, 3mM cysteine, pH 8.5. The mixture is stirred overnight in the cold and then concentrated about
20 10 fold by ultrafiltration. It is then diluted 3 fold with 10mM Tris, 1.5M urea, pH 9. The pH of this mixture is then adjusted to pH 5 with acetic acid. The precipitate is removed by centrifugation and the supernatant is loaded onto a SP-Sepharose Fast Flow column equilibrated in 20mM NaAc, 100 mM NaCl, pH 5(10mg/ml protein load, room temperature).
25 The protein is eluted off using a 20 column volume gradient in the same buffer ranging from 100mM NaCl to 500mM NaCl. The pool from the column is diluted 3 fold and loaded onto a SP-Sepharose HP column in 20 mM NaAc, 150 mM NaCl, pH 5(10 mg/ml protein load, room temperature). The protein is eluted off using a 20 column volume gradient

in the same buffer ranging from 150 mM NaCl to 400 mM NaCl. The peak is pooled and filtered.

Characterization of Fc-TMP activity. The following is a summary of in vivo data in mice with various compounds of this invention.

5 Mice: Normal female BDF1 approximately 10-12 weeks of age.

Bleed schedule: Ten mice per group treated on day 0, two groups started 4 days apart for a total of 20 mice per group. Five mice bled at each time point, mice were bled a minimum of three times a week. Mice were anesthetized with isoflurane and a total volume of 140-160 μ l of blood was
10 obtained by puncture of the orbital sinus. Blood was counted on a Technicon H1E blood analyzer running software for murine blood. Parameters measured were white blood cells, red blood cells, hematocrit, hemoglobin, platelets, neutrophils.

Treatments: Mice were either injected subcutaneously for a bolus
15 treatment or implanted with 7-day micro-osmotic pumps for continuous delivery. Subcutaneous injections were delivered in a volume of 0.2 ml. Osmotic pumps were inserted into a subcutaneous incision made in the skin between the scapulae of anesthetized mice. Compounds were diluted in PBS with 0.1% BSA. All experiments included one control group,
20 labeled "carrier" that were treated with this diluent only. The concentration of the test articles in the pumps was adjusted so that the calibrated flow rate from the pumps gave the treatment levels indicated in the graphs.

Compounds: A dose titration of the compound was delivered to
25 mice in 7 day micro-osmotic pumps. Mice were treated with various compounds at a single dose of 100 μ g/kg in 7 day osmotic pumps. Some of the same compounds were then given to mice as a single bolus injection.

Activity test results: The results of the activity experiments are shown in Figures 11 and 12. In dose response assays using 7-day micro-

osmotic pumps, the maximum effect was seen with the compound of SEQ ID NO: 18 was at 100 $\mu\text{g/kg/day}$; the 10 $\mu\text{g/kg/day}$ dose was about 50% maximally active and 1 $\mu\text{g/kg/day}$ was the lowest dose at which activity could be seen in this assay system. The compound at 10 $\mu\text{g/kg/day}$ dose was about equally active as 100 $\mu\text{g/kg/day}$ unpegylated rHu-MGDF in the same experiment.

Example 3**Fc-EMP fusions**

Fc-EMP. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a monomer of the EPO-mimetic peptide was constructed using standard PCR technology. Templates for PCR reactions were a vector containing the Fc sequence (pFc-A3, described in International application WO 97/23614, published July 3, 1997) and a synthetic gene encoding EPO monomer. The synthetic gene for the monomer was constructed from the 4 overlapping oligonucleotides (SEQ ID NOS: 390 to 393, respectively) shown below:

```

1798-2 TAT GAA AGG TGG AGG TGG TGG TGG AGG TAC TTA CTC TTG
      CCA CTT CGG CCC GCT GAC TTG G
1798-3 CGG TTT GCA AAC CCA AGT CAG CGG GCC GAA GTG GCA AGA
      GTA AGT ACC TCC ACC ACC ACC TCC ACC TTT CAT
1798-4 GTT TGC AAA CCG CAG GGT GGC GGC GGC GGC GGC GGT GGT
      ACC TAT TCC TGT CAT TTT
1798-5 CCA GGT CAG CGG GCC AAA ATG ACA GGA ATA GGT ACC ACC
      GCC GCC GCC GCC GCC ACC CTG

```

The 4 oligonucleotides were annealed to form the duplex encoding an amino acid sequence (SEQ ID NOS: 394 and 395, respectively) shown below:

```

      TATGAAAGGTGGAGGTGGTGGTGGAGGTACTTACTCTTGCCACTTCGGCCCGCTGACTTG
1  -----+-----+-----+-----+-----+ 60
30  TACTTTCCACCTCCACCACCACCTCCATGAATGAGAACGGTGAAGCCGGGCGACTGAAC
   b  M K G G G G G G G T Y S C H F G P L T W -
      GGTTTGCAAACCGCAGGGTGGCGGCGGCGGCGGCGGTGCTACCTATTCCTGTCATTTT
61  -----+-----+-----+-----+-----+ 133
35  CCAAACGTTTGGCGTCCACCGCGCGCGCGCGCCACCATGGATAAGGACAGTAAACCGGCGACTGGACC
   b  V C K P Q G G G G G G G G T Y S C H F -

```

This duplex was amplified in a PCR reaction using

```

1798-18      GCA GAA GAG CCT CTC CCT GTC TCC GGG TAA
             AGG TGG AGG TGG TGG TGG AGG TAC TTA
             CTC T

```

and

```

1798-19      CTA ATT GGA TCC ACG AGA TTA ACC ACC
             CTG CGG TTT GCA A

```

as the sense and antisense primers (SEQ ID NOS: 396 and 397, respectively).

The Fc portion of the molecule was generated in a PCR reaction with pFc-A3 using the primers

5
1216-52 AAC ATA AGT ACC TGT AGG ATC G
1798-17 AGA GTA AGT ACC TCC ACC ACC ACC TCC ACC TTT ACC CGG
10 AGA CAG GGA GAG GCT CTT CTG C

10 which are SEQ ID NOS: 398 and 399, respectively. The oligonucleotides 1798-17 and 1798-18 contain an overlap of 61 nucleotides, allowing the two genes to be fused together in the correct reading frame by combining the above PCR products in a third reaction using the outside primers, 1216-52
15 and 1798-19.

The final PCR gene product (the full length fusion gene) was digested with restriction endonucleases XbaI and BamHI, and then ligated into the vector pAMG21 (described below), also digested with XbaI and BamHI. Ligated DNA was transformed into competent host cells of E. coli
20 strain 2596 (GM221, described herein). Clones were screened for the ability to produce the recombinant protein product and to possess the gene fusion having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #3718.

The nucleotide and amino acid sequence of the resulting fusion
25 protein (SEQ ID NOS: 15 and 16) are shown in Figure 13.

EMP-Fc. A DNA sequence coding for a monomer of the EPO-mimetic peptide fused in-frame to the Fc region of human IgG1 was constructed using standard PCR technology. Templates for PCR reactions were the pFC-A3a vector and a synthetic gene encoding EPO monomer.
30 The synthetic gene for the monomer was constructed from the 4 overlapping oligonucleotides 1798-4 and 1798-5 (above) and 1798-6 and 1798-7 (SEQ ID NOS: 400 and 401, respectively) shown below:

1798-6 GGC CCG CTG ACC TGG GTA TGT AAG CCA CAA GGG GGT GGG
GGA GGC GGG GGG TAA TCT CGA G

5 1798-7 GAT CCT CGA GAT TAC CCC CCG CCT CCC CCA CCC CCT TGT
GGC TTA CAT AC

The 4 oligonucleotides were annealed to form the duplex encoding an amino acid sequence (SEQ ID NOS: 402 and 403, respectively) shown below:

```

      GTTTGCAAACCGCAGGGTGGCGGCGGCGGCGGCGGTGTTACCTATTCCTGTCATTTTGGC
1  -----+-----+-----+-----+-----+-----+-----+ 60
      GTCCCACCGCCGCCGCCGCCGCCACCATGGATAAGGACAGTAAACCG
15 A      V C K P Q G G G G G G G G T Y S C H F G -
      CCGCTGACCTGGGTATGTAAGCCACAAGGGGGTGGGGGAGGCGGGGGTAATCTCGAG
61 -----+-----+-----+-----+-----+-----+ 122
20 A      GCGGACTGGACCCATACATTCCGGTGTCCCCCACCCTCCGCCCCCATTAGAGCTCCTAG
      P L T W V C K P Q G G G G G G G G *

```

This duplex was amplified in a PCR reaction using

1798-21 TTA TTT CAT ATG AAA GGT GGT AAC TAT TCC TGT CAT TTT
25 and

1798-22 TGG ACA TGT GTG AGT TTT GTC CCC CCC GCC TCC CCC ACC
30 CCC T

as the sense and antisense primers (SEQ ID NOS: 404 and 405, respectively).

The Fc portion of the molecule was generated in a PCR reaction with pFc-A3 using the primers

1798-23 AGG GGG TGG GGG AGG CGG GGG GGA CAA AAC TCA CAC ATG
35 TCC A

and

40 1200-54 GTT ATT GCT CAG CGG TGG CA

which are SEQ ID NOS: 406 and 407, respectively. The oligonucleotides 1798-22 and 1798-23 contain an overlap of 43 nucleotides, allowing the two genes to be fused together in the correct reading frame by combining the above PCR products in a third reaction using the outside primers, 1787-21 and 1200-54.

The final PCR gene product (the full length fusion gene) was digested with restriction endonucleases XbaI and BamHI, and then ligated

into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described above. Clones were screened for the ability to produce the recombinant protein product and to possess the gene fusion having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #3688.

The nucleotide and amino acid sequences (SEQ ID NOS: 17 and 18) of the resulting fusion protein are shown in Figure 14.

EMP-EMP-Fc. A DNA sequence coding for a dimer of the EPO-mimetic peptide fused in-frame to the Fc region of human IgG1 was constructed using standard PCR technology. Templates for PCR reactions were the EMP-Fc plasmid from strain #3688 above and a synthetic gene encoding the EPO dimer. The synthetic gene for the dimer was constructed from the 8 overlapping oligonucleotides (SEQ ID NOS:408 to 415, respectively) shown below:

| | | | | | | | | | | | | | |
|---------|------------|------------|------------|------------|------------|------------|------------|-----|-----|-----|-----|-----|-----|
| 1869-23 | TTT TAG | TTT AAG | ATC GAG | GAT GAA | TTG TAA | ATT AAT | CTA ATG | GAT | TTG | AGT | TTT | AAC | TTT |
| 1869-48 | TAA AA | AAG | TTA | AAA | CTC | AAA | TCT | AGA | ATC | AAA | TCG | ATA | AAA |
| 1871-72 | GGA GTT | GGT TGC | ACT AAA | TAC CCG | TCT | TGC | CAC | TTC | GGC | CCG | CTG | ACT | TGG |
| 1871-73 | AGT ATT | CAG TTA | CGG TTC | GCC CTC | GAA CTT | GTG C | GCA | AGA | GTA | AGT | ACC | TCC | CAT |
| 1871-74 | CAG CAT | GGT TTT | GGC GGC | GGC CCG | GGC CTG | GGC ACC | GGC TGG | GGT | GGT | ACC | TAT | TCC | TGT |
| 1871-75 | AAA ACC | ATG CTG | ACA CGG | GGA TTT | ATA GCA | GGT AAC | ACC CCA | ACC | GCC | GCC | GCC | GCC | GCC |
| 1871-78 | GTA AAA | TGT ACT | AAG CAC | CCA ACA | CAA TGT | GGG CCA | GGT | GGG | GGA | GGC | GGG | GGG | GAC |
| 1871-79 | AGT ACA | TTT TAC | GTC CCA | CCC GGT | CCC CAG | GCC CGG | TCC GCC | CCC | ACC | CCC | TTG | TGG | CTT |

The 8 oligonucleotides were annealed to form the duplex encoding an amino acid sequence (SEQ ID NOS: 416 and 417, respectively) shown below:

1 TTTTATCGATTGATCTAGATTGAGTTTAACTTTTGAAGGAGGAATAAAATATG 60
 -----+-----+-----+-----+-----+
 AAAAAATAGCTAACTAAGATCTAAACTCAAATGAAAATCTTCCTCCTTATTTTATAC
 a M -

```

      GGAGGTACTTACTCTTGCCACTTCGGCCCGCTGACTTGGGTTTGCAAACCGCAGGGTGGC
5   a  61  -----+-----+-----+-----+-----+-----+-----+ 120
      CCTCCATGAATGAGAACGGTGAAGCCGGGCGACTGAACCCAAACGTTGGCGTCCCACCG
      G G T Y S C H F G P L T W V C K P Q G G -
      GGCGGCGGCGGCGGTGGTACCTATTCCTGTCTATTTGGCCCGCTGACCTGGGTATGTAAG
10  a  121 -----+-----+-----+-----+-----+-----+-----+ 180
      CCGCCGCCGCCGCCACCATGGATAAGGACAGTAAAACCGGGCGACTGGACCCATACATTC
      G G G G G G T Y S C H F G P L T W V C K -
      CCACAAGGGGGTGGGGGAGGCGGGGGGACAAACTCACACATGTCCA
15  a  181 -----+-----+-----+-----+-----+-----+ 228
      GGTGTTCCCCCACCCTCCGCCCCCTGTTTGA
      P Q G G G G G G D K T H T C P -

```

This duplex was amplified in a PCR reaction using 1869-23 and 1871-79 (shown above) as the sense and antisense primers.

The Fc portion of the molecule was generated in a PCR reaction with strain 3688 DNA using the primers 1798-23 and 1200-54 (shown above).

The oligonucleotides 1871-79 and 1798-23 contain an overlap of 31 nucleotides, allowing the two genes to be fused together in the correct reading frame by combining the above PCR products in a third reaction using the outside primers, 1869-23 and 1200-54.

The final PCR gene product (the full length fusion gene) was digested with restriction endonucleases XbaI and BamHI, and then ligated into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described for Fc-EMP. Clones were screened for ability to produce the recombinant protein product and possession of the gene fusion having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #3813.

The nucleotide and amino acid sequences (SEQ ID NOS: 19 and 20, respectively) of the resulting fusion protein are shown in Figure 15. There is a silent mutation at position 145 (A to G, shown in boldface) such that the final construct has a different nucleotide sequence than the oligonucleotide 1871-72 from which it was derived.

Fc-EMP-EMP. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a dimer of the EPO-mimetic peptide was

constructed using standard PCR technology. Templates for PCR reactions were the plasmids from strains 3688 and 3813 above.

The Fc portion of the molecule was generated in a PCR reaction with strain 3688 DNA using the primers 1216-52 and 1798-17 (shown above). The EMP dimer portion of the molecule was the product of a second PCR reaction with strain 3813 DNA using the primers 1798-18 (also shown above) and SEQ ID NO: 418, shown below:

1798-20 CTA ATT GGA TCC TCG AGA TTA ACC CCC TTG TGG CTT ACAT

The oligonucleotides 1798-17 and 1798-18 contain an overlap of 61 nucleotides, allowing the two genes to be fused together in the correct reading frame by combining the above PCR products in a third reaction using the outside primers, 1216-52 and 1798-20.

The final PCR gene product (the full length fusion gene) was digested with restriction endonucleases XbaI and BamHI, and then ligated into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described for Fc-EMP. Clones were screened for the ability to produce the recombinant protein product and to possess the gene fusion having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #3822.

The nucleotide and amino acid sequences (SEQ ID NOS: __ and __, respectively) of the fusion protein are shown in Figure 16.

Characterization of Fc-EMP activity. Characterization was carried out in vivo as follows.

Mice: Normal female BDF1 approximately 10-12 weeks of age.

Bleed schedule: Ten mice per group treated on day 0, two groups started 4 days apart for a total of 20 mice per group. Five mice bled at each time point, mice were bled a maximum of three times a week. Mice were anesthetized with isoflurane and a total volume of 140-160 ml of blood was obtained by puncture of the orbital sinus. Blood was counted

on a Technicon H1E blood analyzer running software for murine blood. Parameters measured were WBC, RBC, HCT, HGB, PLT, NEUT, LYMPH.

Treatments: Mice were either injected subcutaneously for a bolus treatment or implanted with 7 day micro-osmotic pumps for continuous delivery. Subcutaneous injections were delivered in a volume of 0.2 ml. Osmotic pumps were inserted into a subcutaneous incision made in the skin between the scapulae of anesthetized mice. Compounds were diluted in PBS with 0.1% BSA. All experiments included one control group, labeled "carrier" that were treated with this diluent only. The concentration of the test articles in the pumps was adjusted so that the calibrated flow rate from the pumps gave the treatment levels indicated in the graphs.

Experiments: Various Fc-conjugated EPO mimetic peptides (EMPs) were delivered to mice as a single bolus injection at a dose of 100 µg/kg. Fc-EMPs were delivered to mice in 7-day micro-osmotic pumps. The pumps were not replaced at the end of 7 days. Mice were bled until day 51 when HGB and HCT returned to baseline levels.

Example 4

TNF- α inhibitors

Fc-TNF- α inhibitors. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a monomer of the TNF- α inhibitory peptide was constructed using standard PCR technology. The Fc and 5 glycine linker portion of the molecule was generated in a PCR reaction with DNA from the Fc-EMP fusion strain #3718 (see Example 3) using the sense primer 1216-52 and the antisense primer 2295-89 (SEQ ID NOS: 1112 and 1113, respectively). The nucleotides encoding the TNF- α inhibitory peptide were provided by the PCR primer 2295-89 shown below:

| | | |
|----|---------|---|
| 30 | 1216-52 | AAC ATA AGT ACC TGT AGG ATC G |
| | 2295-89 | CCG CGG ATC CAT TAC GGA CGG TGA CCC AGA GAG GTG TTT TTG TAG |

TGC GGC AGG AAG TCA CCA CCA CCT CCA CCT TTA CCC

The oligonucleotide 2295-89 overlaps the glycine linker and Fc portion of the template by 22 nucleotides, with the PCR resulting in the two genes
5 being fused together in the correct reading frame.

The PCR gene product (the full length fusion gene) was digested with restriction endonucleases NdeI and BamHI, and then ligated into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described for EMP-Fc herein. Clones were screened for the ability to
10 produce the recombinant protein product and to possess the gene fusion having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #4544.

The nucleotide and amino acid sequences (SEQ ID NOS: 1055 and 1056) of the fusion protein are shown in Figures 19A and 19B.

15 TNF- α inhibitor-Fc. A DNA sequence coding for a TNF- α inhibitory peptide fused in-frame to the Fc region of human IgG1 was constructed using standard PCR technology. The template for the PCR reaction was a plasmid containing an unrelated peptide fused via a five glycine linker to Fc. The nucleotides encoding the TNF- α inhibitory peptide were
20 provided by the sense PCR primer 2295-88, with primer 1200-54 serving as the antisense primer (SEQ ID NOS: 1117 and 407, respectively). The primer sequences are shown below:

25 2295-88 GAA TAA CAT ATG GAC TTC CTG CCG CAC TAC AAA AAC ACC TCT CTG GGT
CAC CGT CCG GGT GGA GGC GGT GGG GAC AAA ACT

30 1200-54 GTT ATT GCT CAG CGG TGG CA

The oligonucleotide 2295-88 overlaps the glycine linker and Fc portion of the template by 24 nucleotides, with the PCR resulting in the two genes being fused together in the correct reading frame.

The PCR gene product (the full length fusion gene) was digested with restriction endonucleases NdeI and BamHI, and then ligated into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described for EMP-Fc herein. Clones were screened for the ability to

- 5 produce the recombinant protein product and to possess the gene fusion having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #4543.

The nucleotide and amino acid sequences (SEQ ID NOS: 1057 and 1058) of the fusion protein are shown in Figures 20A and 20B.

- 10 Expression in E. coli. Cultures of each of the pAMG21-Fc-fusion constructs in E. coli GM221 were grown at 37 °C in Luria Broth medium containing 50 mg/ml kanamycin. Induction of gene product expression from the luxPR promoter was achieved following the addition of the synthetic autoinducer N-(3-oxohexanoyl)-DL-homoserine lactone to the
- 15 culture media to a final concentration of 20 ng/ml. Cultures were incubated at 37 °C for a further 3 hours. After 3 hours, the bacterial cultures were examined by microscopy for the presence of inclusion bodies and were then collected by centrifugation. Refractile inclusion bodies were observed in induced cultures indicating that the Fc-fusions
- 20 were most likely produced in the insoluble fraction in E. coli. Cell pellets were lysed directly by resuspension in Laemmli sample buffer containing 10% β-mercaptoethanol and were analyzed by SDS-PAGE. In each case, an intense coomassie-stained band of the appropriate molecular weight was observed on an SDS-PAGE gel.

- 25 Purification of Fc-peptide fusion proteins. Cells are broken in water (1/10) by high pressure homogenization (2 passes at 14,000 PSI) and inclusion bodies are harvested by centrifugation (4200 RPM in J-6B for 1 hour). Inclusion bodies are solubilized in 6M guanidine, 50mM Tris, 8mM DTT, pH 8.7 for 1 hour at a 1/10 ratio. The solubilized mixture is diluted

20 times into 2M urea, 50 mM tris, 160mM arginine, 3mM cysteine, pH 8.5. The mixture is stirred overnight in the cold and then concentrated about 10 fold by ultrafiltration. It is then diluted 3 fold with 10mM Tris, 1.5M urea, pH 9. The pH of this mixture is then adjusted to pH 5 with acetic acid. The precipitate is removed by centrifugation and the supernatant is loaded onto a SP-Sepharose Fast Flow column equilibrated in 20mM NaAc, 100 mM NaCl, pH 5 (10mg/ml protein load, room temperature). The protein is eluted from the column using a 20 column volume gradient in the same buffer ranging from 100mM NaCl to 500mM NaCl. The pool from the column is diluted 3 fold and loaded onto a SP-Sepharose HP column in 20mM NaAc, 150mM NaCl, pH 5 (10mg/ml protein load, room temperature). The protein is eluted using a 20 column volume gradient in the same buffer ranging from 150mM NaCl to 400mM NaCl. The peak is pooled and filtered.

Characterization of activity of Fc-TNF- α inhibitor and TNF- α inhibitor -Fc. Binding of these peptide fusion proteins to TNF- α can be characterized by BIAcore by methods available to one of ordinary skill in the art who is armed with the teachings of the present specification.

Example 5

IL-1 Antagonists

Fc-IL-1 antagonist. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a monomer of an IL-1 antagonist peptide was constructed using standard PCR technology. The Fc and 5 glycine linker portion of the molecule was generated in a PCR reaction with DNA from the Fc-EMP fusion strain #3718 (see Example 3) using the sense primer 1216-52 and the antisense primer 2269-70 (SEQ ID NOS: 1112 and 1118, respectively). The nucleotides encoding the IL-1 antagonist peptide were provided by the PCR primer 2269-70 shown below:

1216-52 AAC ATA AGT ACC TGT AGG ATC G
 2269-70 CCG CGG ATC CAT TAC AGC GGC AGA GCG TAC GGC TGC CAG TAA CCC
 GGG GTC CAT TCG AAA CCA CCA CCT CCA CCT TTA CCC

5

The oligonucleotide 2269-70 overlaps the glycine linker and Fc portion of the template by 22 nucleotides, with the PCR resulting in the two genes being fused together in the correct reading frame.

10 The PCR gene product (the full length fusion gene) was digested with restriction endonucleases NdeI and BamHI, and then ligated into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described for EMP-Fc herein. Clones were screened for the ability to produce the recombinant protein product and to possess the gene fusion
 15 having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #4506.

The nucleotide and amino acid sequences (SEQ ID NOS: 1059 and 1060) of the fusion protein are shown in Figures 21A and 21B.

20 IL-1 antagonist-Fc. A DNA sequence coding for an IL-1 antagonist peptide fused in-frame to the Fc region of human IgG1 was constructed using standard PCR technology. The template for the PCR reaction was a plasmid containing an unrelated peptide fused via a five glycine linker to Fc. The nucleotides encoding the IL-1 antagonist peptide were provided by the sense PCR primer 2269-69, with primer 1200-54 serving as the
 25 antisense primer (SEQ ID NOS: 1119 and 407, respectively). The primer sequences are shown below:

30 2269-69 GAA TAA CAT ATG TTC GAA TGG ACC CCG GGT TAC TGG CAG CCG TAC GCT
 CTG CCG CTG GGT GGA GGC GGT GGG GAC AAA ACT
 1200-54 GTT ATT GCT CAG CGG TGG CA

The oligonucleotide 2269-69 overlaps the glycine linker and Fc portion of the template by 24 nucleotides, with the PCR resulting in the two genes being fused together in the correct reading frame.

5 The PCR gene product (the full length fusion gene) was digested with restriction endonucleases NdeI and BamHI, and then ligated into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described for EMP-Fc herein. Clones were screened for the ability to produce the recombinant protein product and to possess the gene fusion
10 having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #4505.

The nucleotide and amino acid sequences (SEQ ID NOS: 1061 and 1062) of the fusion protein are shown in Figures 22A and 22B. Expression and purification were carried out as in previous examples.

15 Characterization of Fc-IL-1 antagonist peptide and IL-1 antagonist peptide-Fc activity. IL-1 Receptor Binding competition between IL-1 β , IL-1RA and Fc-conjugated IL-1 peptide sequences was carried out using the IGEN system. Reactions contained 0.4 nM biotin-IL-1R + 15 nM IL-1-TAG + 3 uM competitor + 20 ug/ml streptavidin-conjugate beads, where
20 competitors were IL-1RA, Fc-IL-1 antagonist, IL-1 antagonist-Fc). Competition was assayed over a range of competitor concentrations from 3 uM to 1.5 pM. The results are shown in Table C below:

Table C—Results from IL-1 Receptor Binding Competition Assay

| | | <i>IL-1pep-Fc</i> | <i>Fc-IL-1pep</i> | <i>IL-1ra</i> |
|----|---------------------------------|-------------------|-------------------|-----------------|
| 5 | KI | 281.5 | 59.58 | 1.405 |
| | EC50 | 530.0 | 112.2 | 2.645 |
| | 95% Confidence Intervals | | | |
| 10 | EC50 | 280.2 to 1002 | 54.75 to 229.8 | 1.149 to 6.086 |
| | KI | 148.9 to 532.5 | 29.08 to 122.1 | 0.6106 to 3.233 |
| 15 | Goodness of Fit | | | |
| | R² | 0.9790 | 0.9687 | 0.9602 |

Example 6

VEGF-Antagonists

Fc-VEGF Antagonist. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a monomer of the VEGF mimetic peptide was constructed using standard PCR technology. The templates for the PCR reaction were the pFc-A3 plasmid and a synthetic VEGF mimetic peptide gene. The synthetic gene was assembled by annealing the following two oligonucleotides primer (SEQ ID NOS: 1120 and 1121, respectively):

| | | |
|---------|--|-------------------------------------|
| 2293-11 | GTT GAA CCG AAC TGT TGT TTT GAA CGT CTG | GAC ATC CAT GTT ATG TGG GAA TGG GAA |
| 2293-12 | CAG ACG TTC AAA ACA ACA GTT CGG TTC AAC | TTC CCA TTC CCA CAT AAC ATG GAT GTC |

The two oligonucleotides anneal to form the following duplex encoding an amino acid sequence shown below (SEQ ID NOS 1122):

20

GTTGAACCGAACTGTGACATCCATGTTATGTGGGAATGGGAATGTTTTGAACGTCTG

1 -----+-----+-----+-----+-----+----- 57

CAACTTGGCTTGACACTGTAGGTACAATACACCCTTACCCTTACAAAACCTGCAGAC

25 a V E P N C D I H V M W E W E C F E R L

This duplex was amplified in a PCR reaction using 2293-05 and 2293-06 as the sense and antisense primers (SEQ ID NOS. 1125 and 1126).

30 The Fc portion of the molecule was generated in a PCR reaction with the pFc-A3 plasmid using the primers 2293-03 and 2293-04 as the sense and antisense primers (SEQ ID NOS. 1123 and 1124, respectively). The full length fusion gene was obtained from a third PCR reaction using the outside primers 2293-03 and 2293-06. These primers are shown below:

2293-03 ATT TGA TTC TAG AAG GAG GAA TAA CAT ATG GAC AAA ACT CAC
ACA TGT

5 2293-04 GTC ACA GTT CGG TTC AAC ACC ACC ACC ACC ACC TTT ACC CGG
AGA CAG GGA

2293-05 TCC CTG TCT CCG GGT AAA GGT GGT GGT GGT GGT GTT GAA CCG
AAC TGT GAC ATC

10 2293-06 CCG CGG ATC CTC GAG TTA CAG ACG TTC AAA ACA TTC CCA

The PCR gene product (the full length fusion gene) was digested with restriction endonucleases NdeI and BamHI, and then ligated into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described for EMP-Fc herein. Clones were screened for the ability to produce the recombinant protein product and to possess the gene fusion having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #4523.

20 The nucleotide and amino acid sequences (SEQ ID NOS: 1063 and 1064) of the fusion protein are shown in Figures 23A and 23B.

VEGF antagonist -Fc. A DNA sequence coding for a VEGF mimetic peptide fused in-frame to the Fc region of human IgG1 was constructed using standard PCR technology. The templates for the PCR reaction were the pFc-A3 plasmid and the synthetic VEGF mimetic peptide gene described above. The synthetic duplex was amplified in a PCR reaction using 2293-07 and 2293-08 as the sense and antisense primers (SEQ ID NOS. 1127 and 1128, respectively).

30 The Fc portion of the molecule was generated in a PCR reaction with the pFc-A3 plasmid using the primers 2293-09 and 2293-10 as the sense and antisense primers (SEQ ID NOS. 1129 and 1130, respectively).

The full length fusion gene was obtained from a third PCR reaction using the outside primers 2293-07 and 2293-10. These primers are shown below:

5 2293 - 07 ATT TGA TTC TAG AAG GAG GAA TAA CAT ATG GTT GAA CCG AAC
 TGT GAC

 2293 - 08 ACA TGT GTG AGT TTT GTC ACC ACC ACC ACC ACC CAG ACG TTC
 AAA ACA TTC

10 2293 - 09 GAA TGT TTT GAA CGT CTG GGT GGT GGT GGT GGT GAC AAA ACT
 CAC ACA TGT

 2293 - 10 CCG CGG ATC CTC GAG TTA TTT ACC CGG AGA CAG GGA GAG

 The PCR gene product (the full length fusion gene) was digested
15 with restriction endonucleases NdeI and BamHI, and then ligated into the
vector pAMG21 and transformed into competent E. coli strain 2596 cells as
described for EMP-Fc herein. Clones were screened for the ability to
produce the recombinant protein product and to possess the gene fusion
having the correct nucleotide sequence. A single such clone was selected
20 and designated Amgen strain #4524.

 The nucleotide and amino acid sequences (SEQ ID NOS: 1065 and
1066) of the fusion protein are shown in Figures 24A and 24B. Expression
and purification were carried out as in previous examples.

25

Example 7

MMP Inhibitors

Fc-MMP inhibitor. A DNA sequence coding for the Fc region of
human IgG1 fused in-frame to a monomer of an MMP inhibitory peptide
was constructed using standard PCR technology. The Fc and 5 glycine
30 linker portion of the molecule was generated in a PCR reaction with DNA
from the Fc-TNF- α inhibitor fusion strain #4544 (see Example 4) using the
sense primer 1216-52 and the antisense primer 2308-67 (SEQ ID NOS: 1112

and 1131, respectively). The nucleotides encoding the MMP inhibitor peptide were provided by the PCR primer 2308-67 shown below:

5 1216-52 AAC ATA AGT ACC TGT AGG ATC G
 2308-67 CCG CGG ATC CAT TAG CAC AGG GTG AAA CCC CAG TGG GTG GTG
 CAA CCA CCA CCT CCA CCT TTA CCC

10 The oligonucleotide 2308-67 overlaps the glycine linker and Fc portion of the template by 22 nucleotides, with the PCR resulting in the two genes being fused together in the correct reading frame.

15 The PCR gene product (the full length fusion gene) was digested with restriction endonucleases NdeI and BamHI, and then ligated into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described for EMP-Fc herein. Clones were screened for the ability to produce the recombinant protein product and to possess the gene fusion having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #4597.

20 The nucleotide and amino acid sequences (SEQ ID NOS: 1067 and 1068) of the fusion protein are shown in Figures 25A and 25B. Expression and purification were carried out as in previous examples.

25 MMP Inhibitor-Fc. A DNA sequence coding for an MMP inhibitory peptide fused in-frame to the Fc region of human IgG1 was constructed using standard PCR technology. The Fc and 5 glycine linker portion of the molecule was generated in a PCR reaction with DNA from the Fc-TNF- α inhibitor fusion strain #4543 (see Example 4). The nucleotides encoding the MMP inhibitory peptide were provided by the sense PCR primer 2308-66, with primer 1200-54 serving as the antisense primer (SEQ ID NOS: 1132 and 407, respectively). The primer sequences are shown below:

30 2308-66 GAA TAA CAT ATG TGC ACC ACC CAC TGG GGT TTC ACC CTG TGC
 GGT GGA GGC GGT GGG GAC AAA
 35 1200-54 GTT ATT GCT CAG CGG TGG CA

The oligonucleotide 2269-69 overlaps the glycine linker and Fc portion of the template by 24 nucleotides, with the PCR resulting in the two genes being fused together in the correct reading frame.

5 The PCR gene product (the full length fusion gene) was digested with restriction endonucleases NdeI and BamHI, and then ligated into the vector pAMG21 and transformed into competent E. coli strain 2596 cells as described for EMP-Fc herein. Clones were screened for the ability to produce the recombinant protein product and to possess the gene fusion
10 having the correct nucleotide sequence. A single such clone was selected and designated Amgen strain #4598.

The nucleotide and amino acid sequences (SEQ ID NOS: 1069 and 1070) of the fusion protein are shown in Figures 26A and 26B.

* * *

15 The invention now being fully described, it will be apparent to one of ordinary skill in the art that many changes and modifications can be made thereto, without departing from the spirit and scope of the invention as set forth herein.

20

Abbreviations

Abbreviations used throughout this specification are as defined below, unless otherwise defined in specific circumstances.

| | | |
|----|-------|---|
| | Ac | acetyl (used to refer to acetylated residues) |
| | AcBpa | acetylated p-benzoyl-L-phenylalanine |
| 25 | ADCC | antibody-dependent cellular cytotoxicity |
| | Aib | aminoisobutyric acid |
| | bA | beta-alanine |
| | Bpa | p-benzoyl-L-phenylalanine |
| | BrAc | bromoacetyl (BrCH ₂ C(O)) |

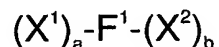
| | | |
|----|----------|---|
| | BSA | Bovine serum albumin |
| | Bzl | Benzyl |
| | Cap | Caproic acid |
| | CTL | Cytotoxic T lymphocytes |
| 5 | CTLA4 | Cytotoxic T lymphocyte antigen 4 |
| | DARC | Duffy blood group antigen receptor |
| | DCC | Dicyclohexylcarbodiimide |
| | Dde | 1-(4,4-dimethyl-2,6-dioxo-cyclohexylidene)ethyl |
| | EMP | Erythropoietin-mimetic peptide |
| 10 | ESI-MS | Electron spray ionization mass spectrometry |
| | EPO | Erythropoietin |
| | Fmoc | fluorenylmethoxycarbonyl |
| | G-CSF | Granulocyte colony stimulating factor |
| | GH | Growth hormone |
| 15 | HCT | hematocrit |
| | HGB | hemoglobin |
| | hGH | Human growth hormone |
| | HOBt | 1-Hydroxybenzotriazole |
| | HPLC | high performance liquid chromatography |
| 20 | IL | interleukin |
| | IL-R | interleukin receptor |
| | IL-1R | interleukin-1 receptor |
| | IL-1ra | interleukin-1 receptor antagonist |
| | Lau | Lauric acid |
| 25 | LPS | lipopolysaccharide |
| | LYMPH | lymphocytes |
| | MALDI-MS | Matrix-assisted laser desorption ionization mass spectrometry |
| | Me | methyl |

| | | |
|----|-------|---|
| | MeO | methoxy |
| | MHC | major histocompatibility complex |
| | MMP | matrix metalloproteinase |
| | MMPI | matrix metalloproteinase inhibitor |
| 5 | 1-Nap | 1-naphthylalanine |
| | NEUT | neutrophils |
| | NGF | nerve growth factor |
| | Nle | norleucine |
| | NMP | N-methyl-2-pyrrolidinone |
| 10 | PAGE | polyacrylamide gel electrophoresis |
| | PBS | Phosphate-buffered saline |
| | Pbf | 2,2,4,6,7-pendamethyldihydrobenzofuran-5-sulfonyl |
| | PCR | polymerase chain reaction |
| | Pec | pipecolic acid |
| 15 | PEG | Poly(ethylene glycol) |
| | pGlu | pyroglutamic acid |
| | Pic | picolinic acid |
| | PLT | platelets |
| | pY | phosphotyrosine |
| 20 | RBC | red blood cells |
| | RBS | ribosome binding site |
| | RT | room temperature (25 °C) |
| | Sar | sarcosine |
| | SDS | sodium dodecyl sulfate |
| 25 | STK | serine-threonine kinases |
| | t-Boc | tert-Butoxycarbonyl |
| | tBu | tert-Butyl |
| | TGF | tissue growth factor |
| | THF | thymic humoral factor |

| | | |
|----|-------|---|
| | TK | tyrosine kinase |
| | TMP | Thrombopoietin-mimetic peptide |
| | TNF | Tissue necrosis factor |
| | TPO | Thrombopoietin |
| 5 | TRAIL | TNF-related apoptosis-inducing ligand |
| | Trt | trityl |
| | UK | urokinase |
| | UKR | urokinase receptor |
| | VEGF | vascular endothelial cell growth factor |
| 10 | VIP | vasoactive intestinal peptide |
| | WBC | white blood cells |

What is claimed is:

1. A composition of matter of the formula



and multimers thereof, wherein:

5

F^1 is an Fc domain;

X^1 and X^2 are each independently selected from $-(L^1)_c-P^1$, $-(L^1)_c-P^1-(L^2)_d-P^2$, $-(L^1)_c-P^1-(L^2)_d-P^2-(L^3)_e-P^3$, and $-(L^1)_c-P^1-(L^2)_d-P^2-(L^3)_e-P^3-(L^4)_f-P^4$

10

P^1 , P^2 , P^3 , and P^4 are each independently sequences of pharmacologically active peptides;

L^1 , L^2 , L^3 , and L^4 are each independently linkers; and

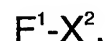
a , b , c , d , e , and f are each independently 0 or 1, provided that at least one of a and b is 1.

2. The composition of matter of Claim 1 of the formulae

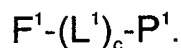
15



or

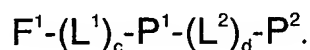


3. The composition of matter of Claim 1 of the formula



20

4. The composition of matter of Claim 1 of the formula



5. The composition of matter of Claim 1 wherein F^1 is an IgG Fc domain.

6. The composition of matter of Claim 1 wherein F^1 is an IgG1 Fc domain.

25

7. The composition of matter of Claim 1 wherein F^1 comprises the sequence of SEQ ID NO: 2.

8. The composition of matter of Claim 1 wherein X^1 and X^2 comprise an IL-1 antagonist peptide sequence.

9. The composition of matter of Claim 8 wherein the IL-1 antagonist peptide sequence is selected from SEQ ID NOS: 212, 907, 908, 909, 910, 917, and 979.
10. The composition of matter of Claim 8 wherein the IL-1 antagonist peptide sequence is selected from SEQ ID NOS: 213 to 271, 671 to 906, 911 to 916, and 918 to 1023.
11. The composition of matter of Claim 8 wherein F¹ comprises the sequence of SEQ ID NO: 2.
12. The composition of matter of Claim 1 wherein X¹ and X² comprise an EPO-mimetic peptide sequence.
13. The composition of matter of Claim 12 wherein the EPO-mimetic peptide sequence is selected from Table 5.
14. The composition of matter of Claim 12 wherein F¹ comprises the sequence of SEQ ID NO: 2.
15. 15. The composition of matter of Claim 12 comprising a sequence selected from SEQ ID NOS: 83, 84, 85, 124, 419, 420, 421, and 461. .
16. The composition of matter of claim 12 comprising a sequence selected from SEQ ID NOS: 339 and 340.
17. The composition of matter of Claim 12 comprising a sequence selected from SEQ ID NOS: 20 and 22.
18. The composition of matter of Claim 3 wherein P¹ is a TPO-mimetic peptide sequence.
19. The composition of matter of Claim 18 wherein P¹ is a TPO-mimetic peptide sequence selected from Table 6.
20. 20. The composition of matter of Claim 18 wherein F¹ comprises the sequence of SEQ ID NO: 2.
21. The composition of matter of Claim 18 having a sequence selected from SEQ ID NOS: 6 and 12.
22. A DNA encoding a composition of matter of any of Claims 1 to 21.

23. An expression vector comprising the DNA of Claim 22.
24. A host cell comprising the expression vector of Claim 23.
25. The cell of Claim 24, wherein the cell is an E. coli cell.
26. A process for preparing a pharmacologically active compound,
5 which comprises
- a) selecting at least one randomized peptide that modulates the activity of a protein of interest; and
- b) preparing a pharmacologic agent comprising at least one Fc domain covalently linked to at least one amino acid sequence
10 of the selected peptide or peptides.
27. The process of Claim 26, wherein the peptide is selected in a process comprising screening of a phage display library, an E. coli display library, a ribosomal library, or a chemical peptide library.
28. The process of Claim 26, wherein the preparation of the
15 pharmacologic agent is carried out by:
- a) preparing a gene construct comprising a nucleic acid sequence encoding the selected peptide and a nucleic acid sequence encoding an Fc domain; and
- b) expressing the gene construct.
- 20 29. The process of Claim 26, wherein the gene construct is expressed in an E. coli cell.
30. The process of Claim 26, wherein the protein of interest is a cell surface receptor.
31. The process of Claim 26, wherein the protein of interest has a linear
25 epitope.
32. The process of Claim 26, wherein the protein of interest is a cytokine receptor.
33. The process of Claim 26, wherein the peptide is an EPO-mimetic peptide.

34. The process of Claim 26, wherein the peptide is a TPO-mimetic peptide.
35. The process of Claim 26, wherein the peptide is an IL-1 antagonist peptide.
- 5 36. The process of Claim 26, wherein the peptide is an MMP inhibitor peptide or a VEGF antagonist peptide.
37. The process of Claim 26, wherein the peptide is a TNF-antagonist peptide.
38. The process of Claim 26, wherein the peptide is a CTLA4-mimetic peptide.
- 10 39. The process of Claim 26, wherein the peptide is selected from Tables 4 to 20.
40. The process of Claim 26, wherein the selection of the peptide is carried out by a process comprising:
- 15 a) preparing a gene construct comprising a nucleic acid sequence encoding a first selected peptide and a nucleic acid sequence encoding an Fc domain;
- b) conducting a polymerase chain reaction using the gene construct and mutagenic primers, wherein
- 20 i) a first mutagenic primer comprises a nucleic acid sequence complementary to a sequence at or near the 5' end of a coding strand of the gene construct, and
- ii) a second mutagenic primer comprises a nucleic acid sequence complementary to the 3' end of the noncoding strand of the gene construct.
- 25 41. The process of Claim 26, wherein the compound is derivatized.
42. The process of Claim 26, wherein the derivatized compound comprises a cyclic portion, a cross-linking site, a non-peptidyl

linkage, an N-terminal replacement, a C-terminal replacement, or a modified amino acid moiety.

43. The process of Claim 26 wherein the Fc domain is an IgG Fc domain.

5 44. The process of Claim 26, wherein the vehicle is an IgG1 Fc domain.

45. The process of Claim 26, wherein the vehicle comprises the sequence of SEQ ID NO: 2.

46. The process of Claim 26, wherein the compound prepared is of the formula

$$10 \quad (X^1)_a - F^1 - (X^2)_b$$

and multimers thereof, wherein:

F^1 is an Fc domain;

X^1 and X^2 are each independently selected from $-(L^1)_c - P^1$, $-(L^1)_c - P^1 - (L^2)_d - P^2$, $-(L^1)_c - P^1 - (L^2)_d - P^2 - (L^3)_e - P^3$, and $-(L^1)_c - P^1 - (L^2)_d - P^2 - (L^3)_e - P^3 - (L^4)_f - P^4$

P^1 , P^2 , P^3 , and P^4 are each independently sequences of pharmacologically active peptides;

L^1 , L^2 , L^3 , and L^4 are each independently linkers; and

a , b , c , d , e , and f are each independently 0 or 1, provided

20 that at least one of a and b is 1.

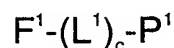
47. The process of Claim 46, wherein the compound prepared is of the formulae



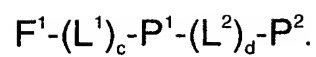
or

$$25 \quad F^1 - X^2.$$

48. The process of Claim 46, wherein the compound prepared is of the formulae



or



49. The process of Claim 46, wherein F^1 is an IgG Fc domain.
50. The process of Claim 46, wherein F^1 is an IgG1 Fc domain.
- 5 51. The process of Claim 46, wherein F^1 comprises the sequence of SEQ
ID NO: 2.

FIG. 1

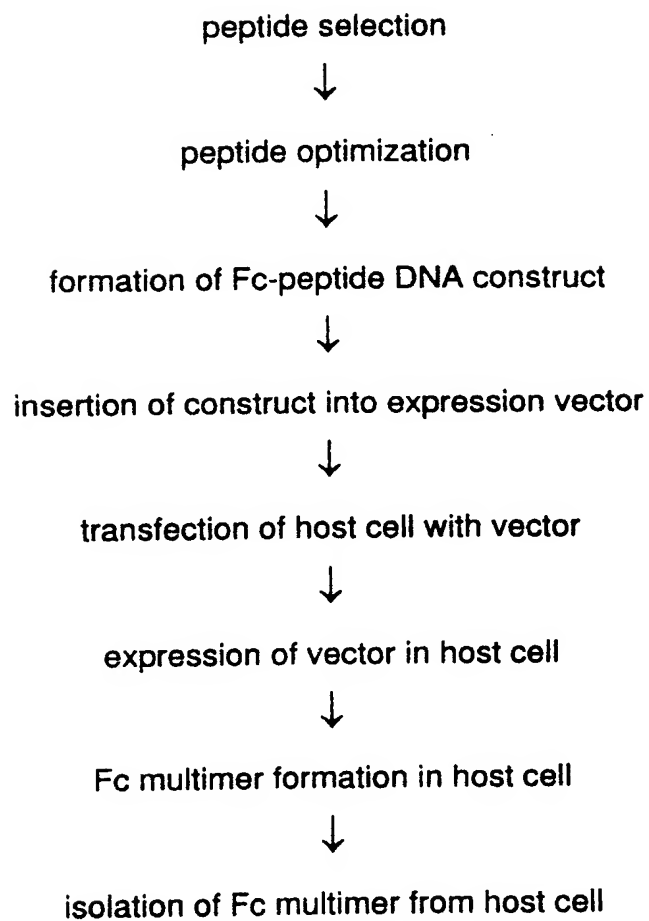


FIG. 2A

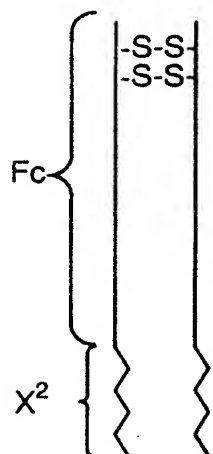


FIG. 2B

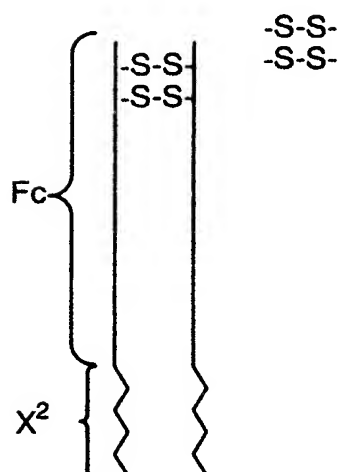


FIG. 2C

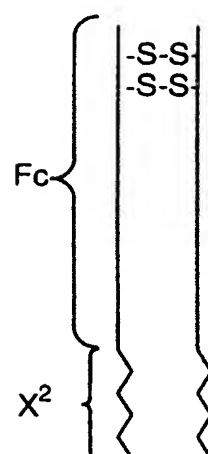


FIG. 2D

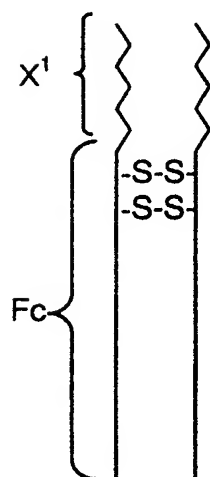


FIG. 2E

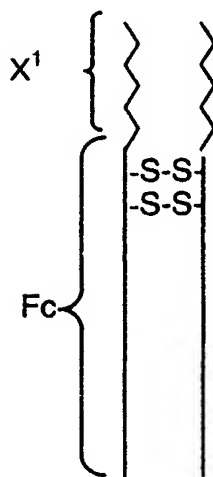


FIG. 2F

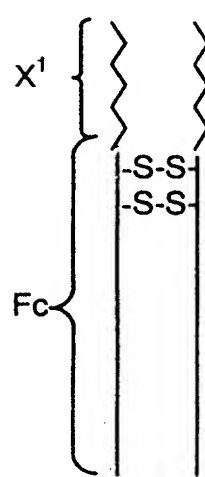


FIG. 3A

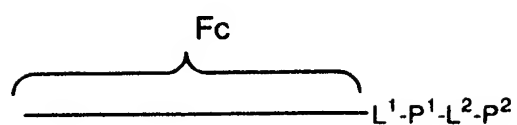


FIG. 3B

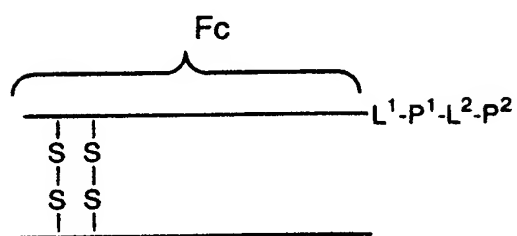


FIG. 3C

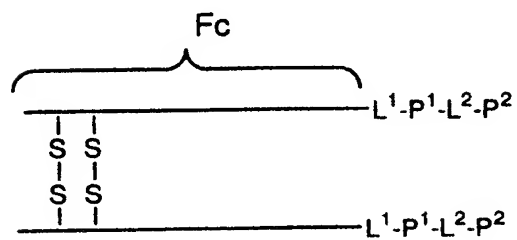


FIG. 4

ATGGACAAAAC TCACACATGTCCACCTTGTCCAGCTCCGGAAC TCCTGGGGGGACCGTCA
1 -----+-----+-----+-----+-----+-----+-----+ 60
TACCTGTTTTGAGTGTGTACAGGTGGAACAGGTCGAGGCCTTGAGGACCCCCCTGGCAGT

a M D K T H T C P P C P A P E L L G G P S -
GTCTTCTCTTCCCCCAAACCCAAGGACACCCCTCATGATCTCCCGGACCCCTGAGGTC
61 -----+-----+-----+-----+-----+-----+ 120
CAGAAGGAGAAGGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAG

a V F L F P P K P K D T L M I S R T P E V -
ACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTG
121 -----+-----+-----+-----+-----+-----+ 180
TGTACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCAC

a T C V V V D V S H E D P E V K F N W Y V -
GACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCAGC
181 -----+-----+-----+-----+-----+-----+ 240
CTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCTGTC

a D G V E V H N A K T K P R E E Q Y N S T -
TACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTAC
241 -----+-----+-----+-----+-----+-----+ 300
ATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATG

a Y R V V S V L T V L H Q D W L N G K E Y -
AAGTGAAGGTCTCCAACAAAGCCCTCCCGAGCCCCATCGAGAAAACCATCTCCAAGCC
301 -----+-----+-----+-----+-----+-----+ 360
TTCACGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGG

a K C K V S N K A L P A P I E K T I S K A -
AAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACC
361 -----+-----+-----+-----+-----+-----+ 420
TTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGACTGG

a K G Q P R E P Q V Y T L P P S R D E L T -
AAGAACCAGGTGAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTG
421 -----+-----+-----+-----+-----+-----+ 480
TTCTTGGTCCAGTCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCAC

a K N Q V S L T C L V K G F Y P S D I A V -
GAGTGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAAGACCACGCCTCCCGTGCTGGAC
481 -----+-----+-----+-----+-----+-----+ 540
CTCACCTCTCGTTACCCGTCGGCCTCTTGTGATGTTCTGGTGGGAGGGCAGCAGCTG

a E W E S N G Q P E N N Y K T T P P V L D -
TCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAG
541 -----+-----+-----+-----+-----+-----+ 600
AGGCTGCCGAGGAAGAAGGAGATGTCGTTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTC

a S D G S F F L Y S K L T V D K S R W Q Q -
GGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAG
601 -----+-----+-----+-----+-----+-----+ 660
CCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGTATGTGCGTCTTC

a G N V F S C S V M H E A L H N H Y T Q K -
AGCCTCTCCCTGTCTCCGGGTAAA
661 -----+-----+-----+-----+-----+ 684
TCGGAGAGGGACAGAGGCCCATTT

FIG. 5

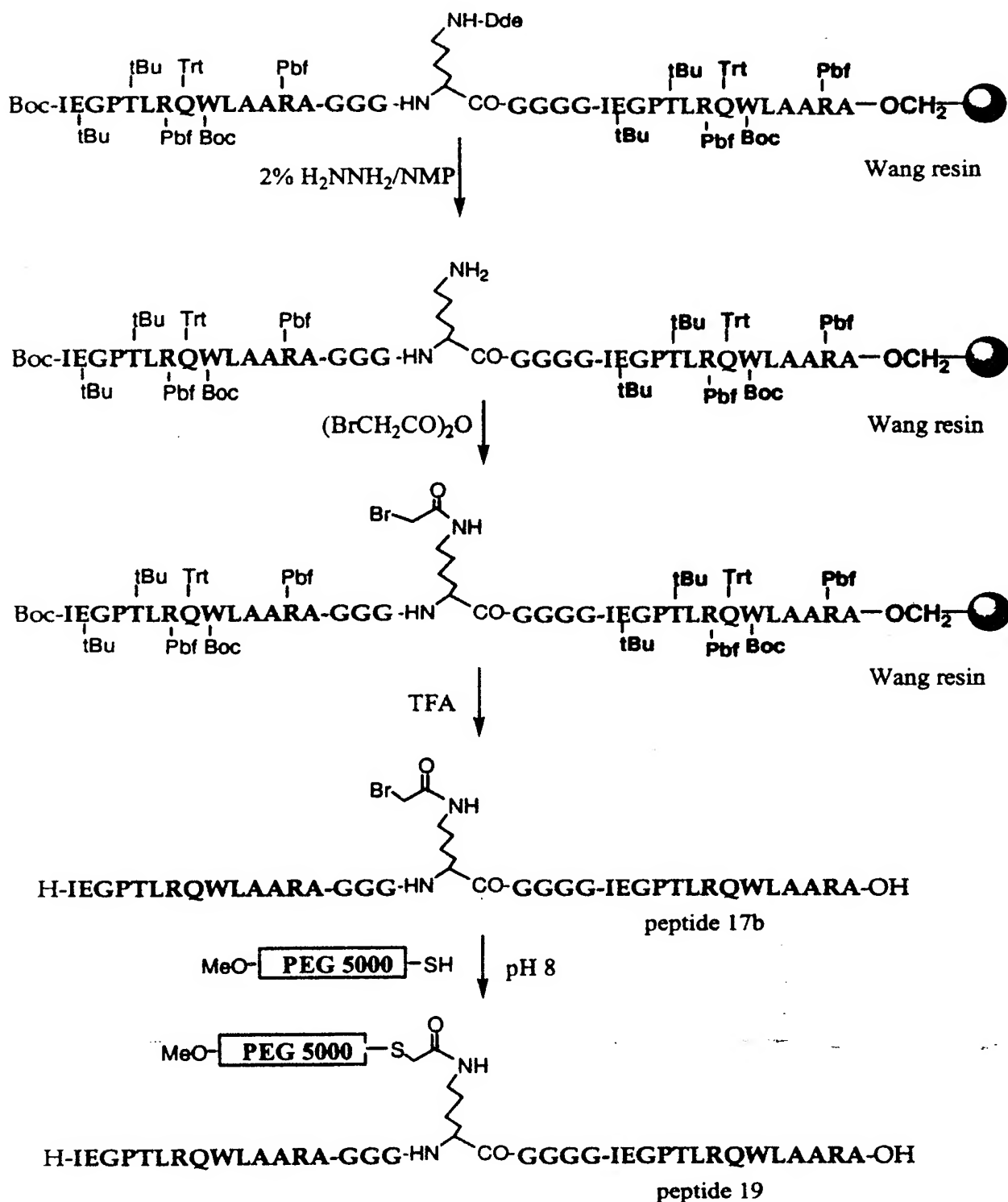


FIG. 6

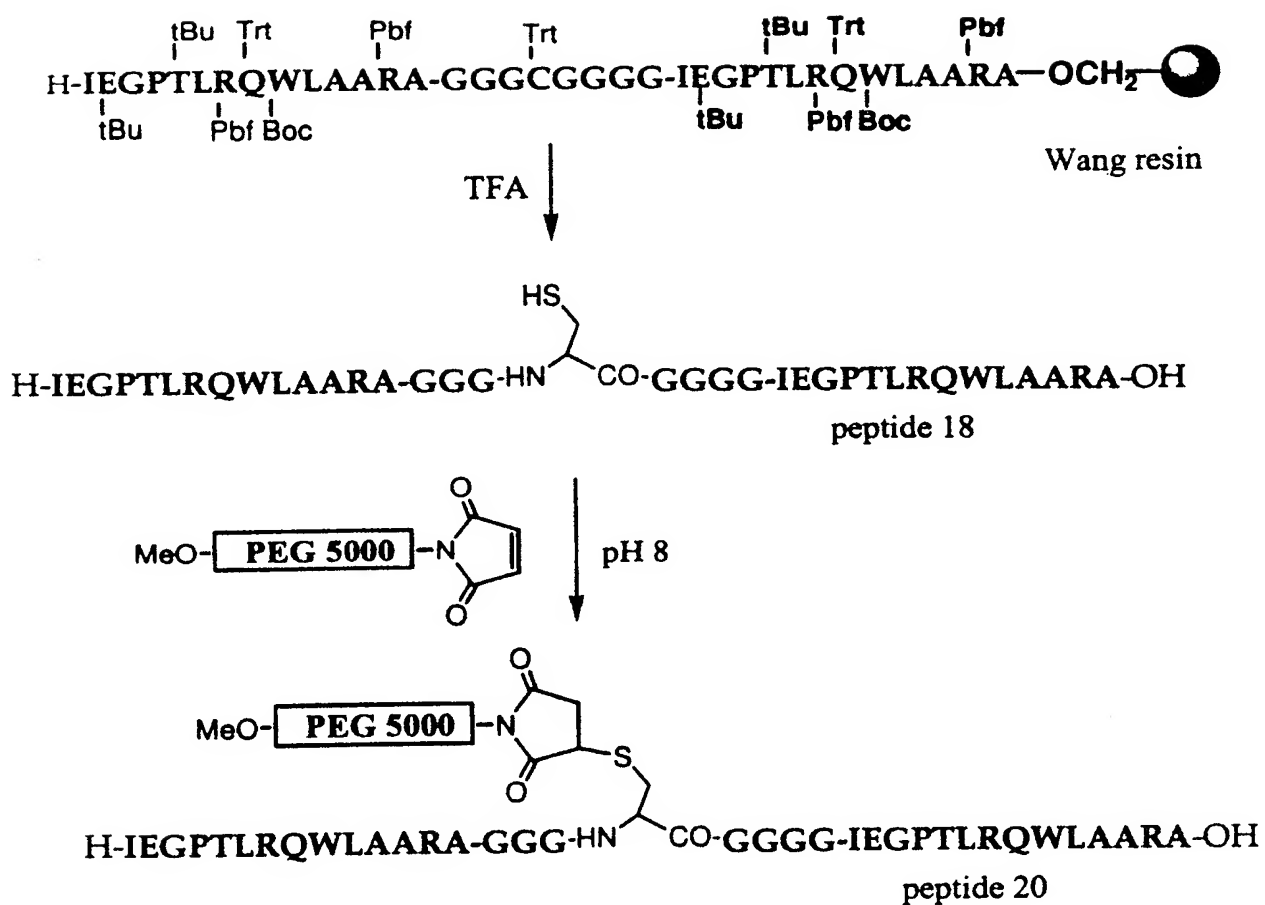


FIG. 7

XbaI
|
1 TCTAGATTTGTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGTC 60
-----+-----+-----+-----+-----+
AGATCTAAACAAAATTGATTAATTCCTCCTTATTGTATACCTGTTTTGAGTGTGTACAG
M D K T H T C P -
c
CACCTTGTCCAGCTCCGGAACCTCTGGGGGACCGTCAGTCTTCCTCTTCCCCCAAAAC
61 -----+-----+-----+-----+-----+ 120
GTGGAACAGGTCGAGGCCTTGAGGACCCCCCTGGCAGTCAGAAGGAGAAGGGGGGTTTTG
P C P A P E L L G G P S V F L F P P K P -
c
CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGA
121 -----+-----+-----+-----+-----+ 180
GGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCACCACCTGCACT
K D T L M I S R T P E V T C V V V D V S -
c
GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATG
181 -----+-----+-----+-----+-----+ 240
CGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTAC
H E D P E V K F N W Y V D G V E V H N A -
c
CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCA
241 -----+-----+-----+-----+-----+ 300
GGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCTGTCATGGCACACCAGTCGCAGGAGT
K T K P R E E Q Y N S T Y R V V S V L T -
c
CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG
301 -----+-----+-----+-----+-----+ 360
GGCAGGACGTGGTCTGACCGACTTACCGTTCCTCATGTTACGTTCCAGAGGTTGTTTC
V L H Q D W L N G K E Y K C K V S N K A -
c
CCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC
361 -----+-----+-----+-----+-----+ 420
GGGAGGGTTCGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGGGGCTCTTGGTG
L P A P I E K T I S K A K G Q P R E P Q -
c
AGGTGTACACCCTGCCCCCATCCCGGATGAGCTGACCAAGAACCAGGTACGCCTGACCT
421 -----+-----+-----+-----+-----+ 480
TCCACATGTGGGACGGGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACTGGA
V Y T L P P S R D E L T K N Q V S L T C -
c
GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGC
481 -----+-----+-----+-----+-----+ 540
CGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCTCTCGTTACCCGTCG
L V K G F Y P S D I A V E W E S N G Q P -
c
CGGAGAACAACATAAGACCACGCCTCCCGTGTGGACTCCGACGGCTCCTTCTTCTCT
541 -----+-----+-----+-----+-----+ 600
GCCTCTTGTGATGTTCTGGTGGGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGGAGA
E N N Y K T T P P V L D S D G S F F L Y -
c
ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG
601 -----+-----+-----+-----+-----+ 660
TGTCGTTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCGAGAAGAGTACGAGGC
S K L T V D K S R W Q Q G N V F S C S V -
c
TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTA
661 -----+-----+-----+-----+-----+ 720
ACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCAT
M H E A L H N H Y T Q K S L S L S P G K -
c
AAGGTGGAGGTGGTGGTATCGAAGGTCCGACTCTGCGTCAGTGGCTGGCTGCTCGTGCTT
721 -----+-----+-----+-----+-----+ 780
TTCCACCTCCACCACCATAGCTTCCAGGCTGAGACGCAGTCACCGACCGACGAGCACGAA
G G G G G I E G P T L R Q W L A A R A * -
c
BamHI
|
AATCTCGAGGATCC
781 -----+----- 794
TTAGAGCTCCTAGG

FIG. 8

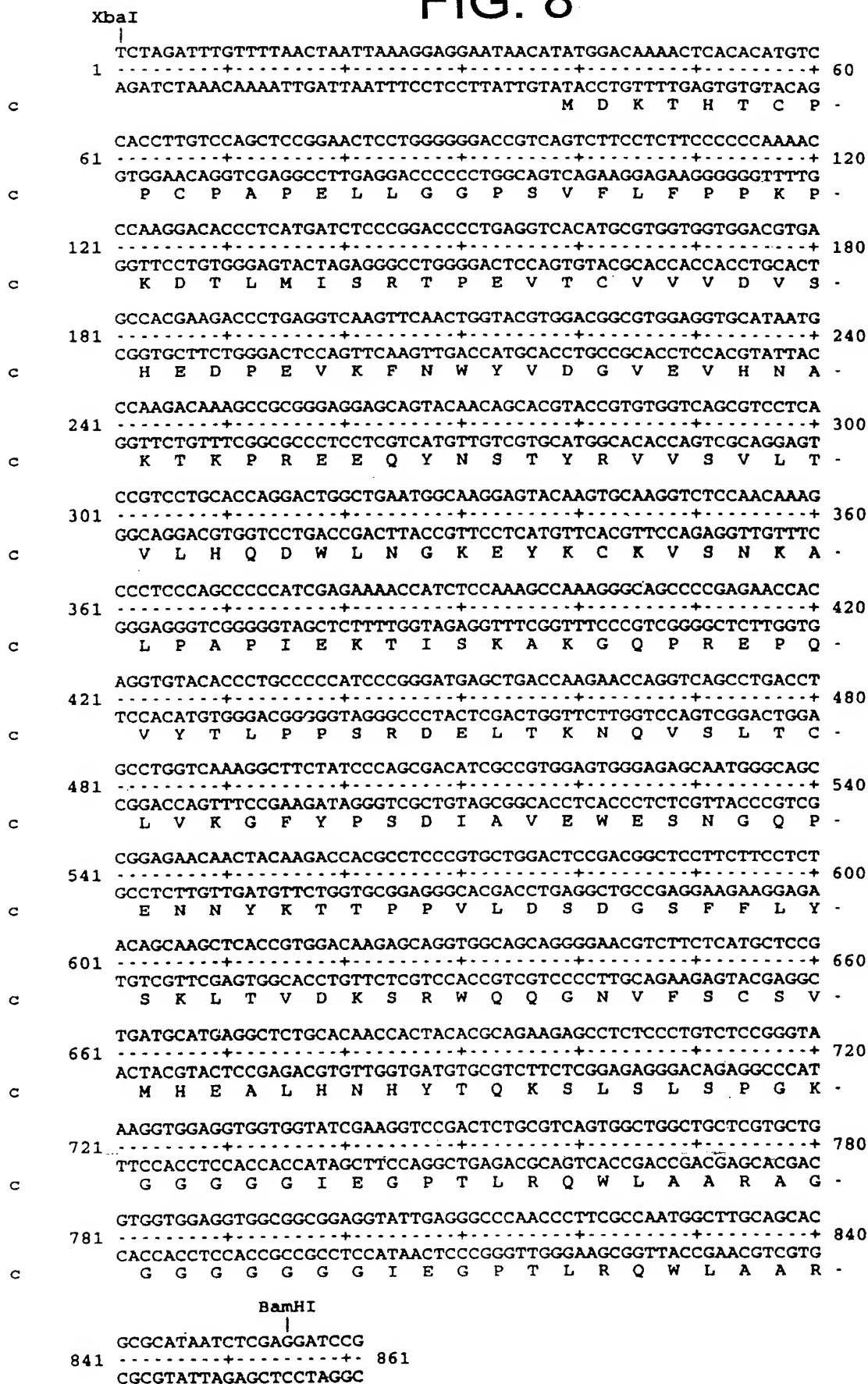


FIG. 9

[illegible]

FIG.11

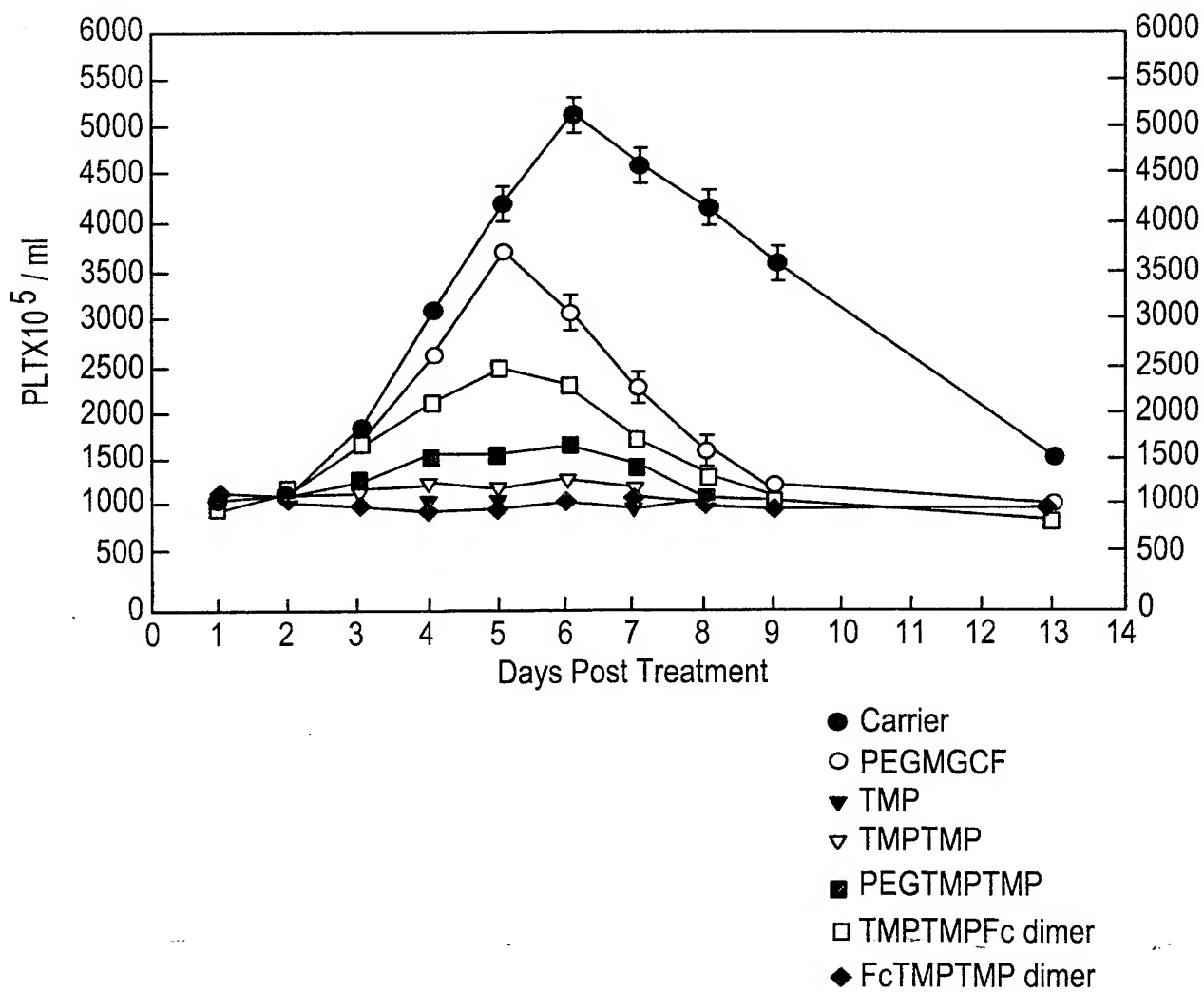


FIG.12

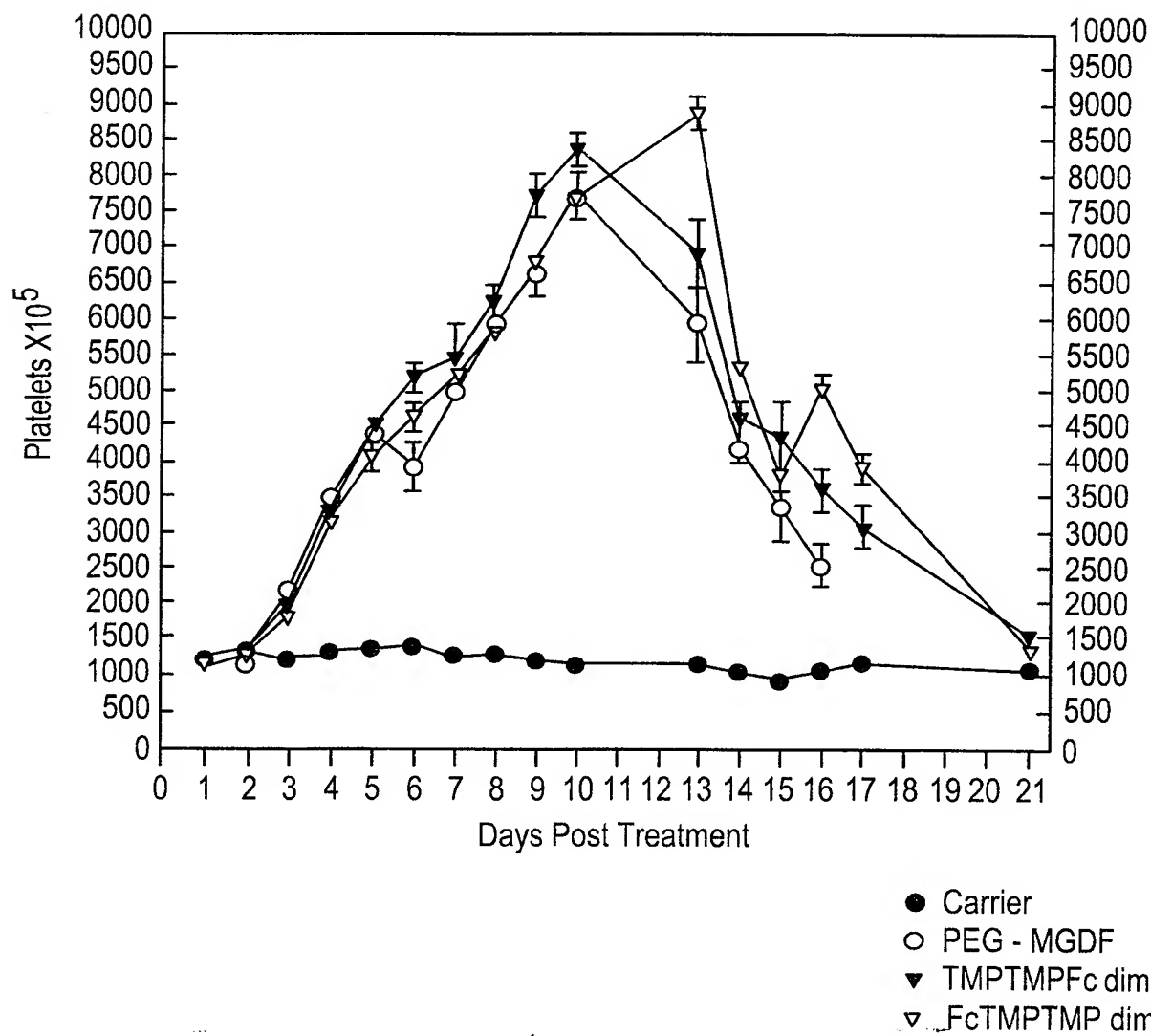


FIG. 13

XbaI
|
1 TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGTC 60
AGATCTAAACAAAATTGATTAATTTCTCTCTTATTGTATACCTGTTTTGAGTGTGTACAG
c M D K T H T C P -
61 CACCTTGTCCAGCTCCGGAACCTCGGGGGACCGTCAGTCTTCTCTTCCCCCAAAAC 120
GTGGAACAGGTCGAGGCCTTGAGGACCCCCCTGGCAGTCAGAAGGAGAAGGGGGGTTTTG
c P C P A P E L L G G P S V F L F P P K P -
121 CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGA 180
GGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCACCACCTGCACT
c K D T L M I S R T P E V T C V V V D V S -
181 GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATG 240
CGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTAC
c H E D P E V K F N W Y V D G V E V H N A -
241 CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCTCTCA 300
GGTTCGTGTTTCGGCGCCCTCCTCGTCATGTTGTGTCATGGCACACCAGTCGAGGAGT
c K T K P R E E Q Y N S T Y R V V S V L T -
301 CCGTCTGCAACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG 360
GGCAGGACGTGGTCTGACCGACTTACCGTTCTCATGTTTACGTTCCAGAGGTTGTTTC
c V L H Q D W L N G K E Y K C K V S N K A -
361 CCCTCCCAGCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC 420
GGGAGGGTCGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGGGGCTCTTGGTG
c L P A P I E K T I S K A K G Q P R E P Q -
421 AGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT 480
TCCACATGTGGGACGGGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACTGGA
c V Y T L P P S R D E L T K N Q V S L T C -
481 GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGC 540
CGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCTCTCGTTACCCGTCG
c L V K G F Y P S D I A V E W E S N G Q P -
541 CGGAGAACAACATAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTCTCTCT 600
GCCTCTTGTGATGTTCTGGTGGGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGGAGA
c E N N Y K T T P P V L D S D G S F F L Y -
601 ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG 660
TGTCGTTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCTTGCAGAAGAGTACGAGGC
c S K L T V D K S R W Q Q G N V F S C S V -
661 TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTA 720
ACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCAT
c M H E A L H N H Y T Q K S L S L S P G K -
721 AAGGTGGAGGTGGTGGTGGAGGTACTTACTCTTGCCACTTCGGCCCGCTGACTTGGGTTT 780
TTCCACCTCCACCACCACCTCCATGAATGAGAACGGTGAAGCCGGGCGACTGAACCCAAA
c G G G G G G G T Y S C H F G P L T W V C -
BamHI
|
781 GCAAACCGCAGGGTGGTTAATCTCGTGGATCC 812
CGTTTGGCGTCCCACCAATTAGAGCACCTAGG
c K P Q G G *

FIG. 14

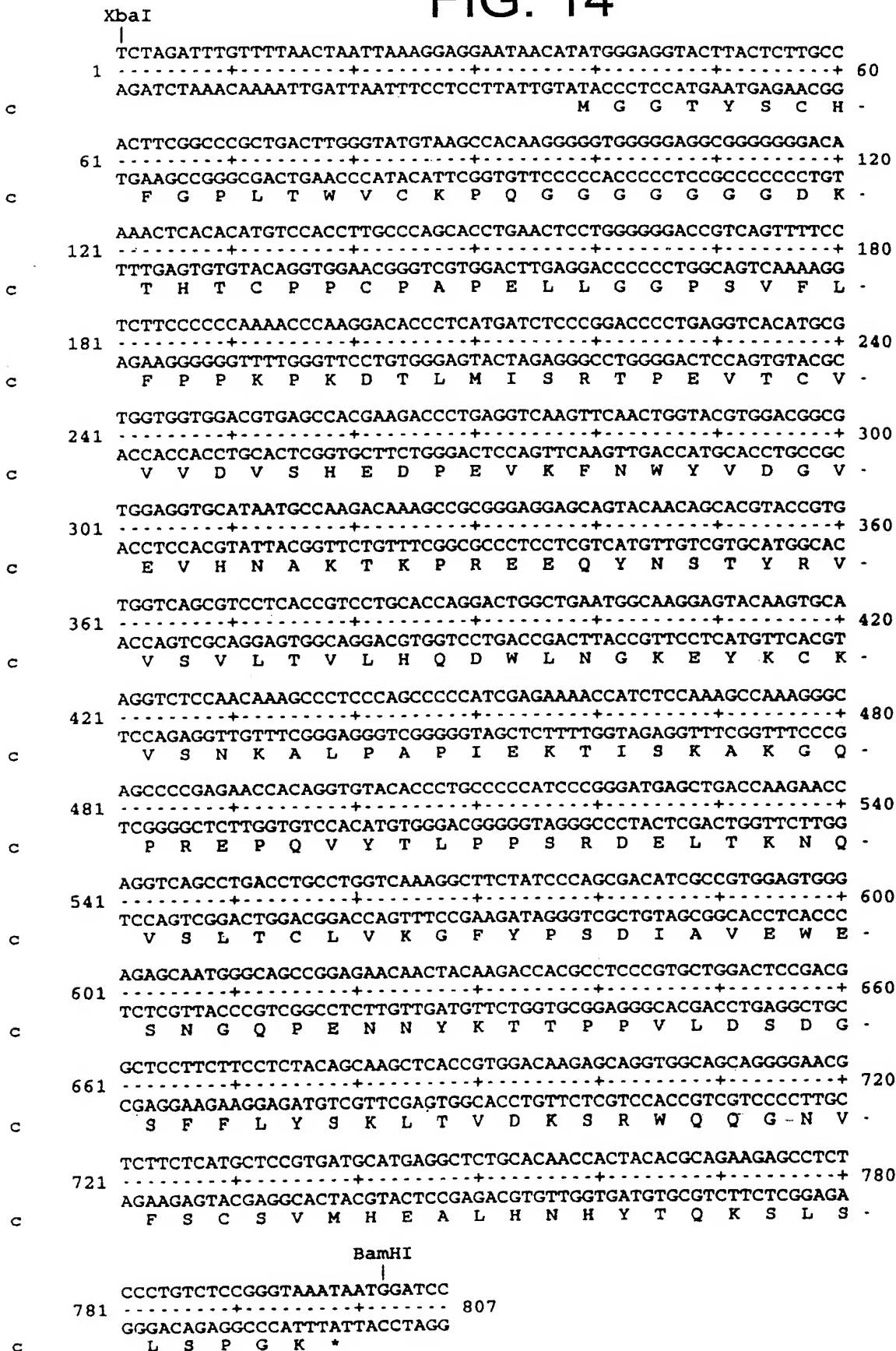


FIG. 16

XbaI
|
TCTAGATTGTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACCTCACACATGTC
1+.....+.....+.....+.....+ 60
AGATCTAAACAAAATTGATTAATTCCTCCTTATTGTATACCTGTTTTGAGTGTGTACAG
c M D K T H T C P -

CACCTTGCCCAGCACCTGAACCTCCTGGGGGACCGTCAGTTTTCTCTTCCCCCAAAAC
61+.....+.....+.....+.....+ 120
GTGGAACGGGTCGTGGACTTGAGGACCCCTGGCAGTCAAAAGGAGAAGGGGGTTTTG
c P C P A P E L L G G P S V F L P P K P -

CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGA
121+.....+.....+.....+.....+ 180
GGTTCCTGTGGGAGTACTAGAGGGCTGGGGACTCCAGTGACGCACCACCACCTGCACT
c K D T L M I S R T P E V T C V V V D V S -

GCCACGAAGACCCTGAGGTCAAGTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATG
181+.....+.....+.....+.....+ 240
CGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTAC
c H E D P E V K F N W Y V D G V E V H N A -

CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCTCTCA
241+.....+.....+.....+.....+ 300
GGTTCGTGTTTCGGCGCCCTCCTCGTCATGTTGTCTGTCATGGCACACCAAGTCGAGGAGT
c K T K P R E E Q Y N S T Y R V V S V L T -

CCGTCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG
301+.....+.....+.....+.....+ 360
GGCAGGACGTGGTCTGACCGACTTACCGTTCTCATGTTTACGTTCCAGAGGTGTTTC
c V L H Q D W L N G K E Y K C K V S N K A -

CCCTCCCAGCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC
361+.....+.....+.....+.....+ 420
GGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCGTCGCGGGCTCTGGTG
c L P A P I E K T I S K A K G Q P R E P Q -

AGGTGTACACCCTGCCTCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT
421+.....+.....+.....+.....+ 480
TCCACATGTGGGACGGAGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACTGGA
c V Y T L P P S R D E L T K N Q V S L T C -

GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGC
481+.....+.....+.....+.....+ 540
CGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCTCTCGTTACCCGTCG
c L V K G F Y P S D I A V E W E S N G Q P -

CGGAGAACAACCTACAAGACCACGCCTCCCGTGTGGACTCCGACGGCTCCTTCTTCTCT
541+.....+.....+.....+.....+ 600
GCCTCTTGTGATGTTCTGGTGCGGAGGGCAGACCTGAGGCTGCCGAGGAAGAAGGAGA
c E N N Y K T T P P V L D S D G S F F L Y -

ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG
601+.....+.....+.....+.....+ 660
TGTCGTTTCGAGTGGACCTGTCTCGTCCACCGTCGTCCCTTGCAGAAGAGTACGAGGC
c S K L T V D K S R W Q Q G N V F S C S V -

TGATGCATGAGGCTCTGCACAACCACTACACGAGAAGAGCCTCTCCCTGTCTCCGGGTA
661+.....+.....+.....+.....+ 720
ACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCAT
c M H E A L H N H Y T Q K S L S L S P G K -

AAGGTGGAGGTGGTGGCGGAGGTACTTACTCTTGCCACTTCGGCCCACTGACTTGGGTTT
721+.....+.....+.....+.....+ 780
TTCCACCTCCACCACCGCCTCCATGAATGAGAACGGTGAAGCCGGGTGACTGAACCCAAA
c G G G G G G G T Y S C H F G P L T W V C -

GCAAACCGCAGGTGGCGGCGCGCGCGCGGTGACCTATTCCTGTCAATTTTGGCCCGC
781+.....+.....+.....+.....+ 840
CGTTTGGCGTCCCACCGCGCGCGCGCGCCACCATGGATAAGGACAGTAAAACCGGGCG
c K P Q G G G G G G G T Y S C H F G P L -

BamHI
|
TGACCTGGGTATGTAAGCCACAAGGGGGTTAATCTCGAGGATCC
841+.....+.....+.....+.....+ 884
ACTGGACCCATACATTGGGTGTTCCCCCAATTAGAGCTCCTAGG
c T W V C K P Q G G *

FIG. 17A

[AatII sticky end] 5' GCGTAACGTATGCATGGTCTCC -
 (position #4358 in pAMG21) 3' TGCACGCATTGCATACGTACCAGAGG -

- CCATGCGAGAGTAGGGAAC TGCCAGGCATCAAATAAAACGAAAGGCTCAGTCGAAAGACT -
 - GGTACGCTCTCATCCCTTGACGGTCCGTAGTTTATTTTGCTTCCGAGTCAGCTTTCTGA -

- GGGCCTTTCGTTTTATCTGTTGTTTGTGCGGTGAACGCTCTCCTGAGTAGGACAAATCCGC -
 - CCCGGAAGCAAAATAGACAACAAACAGCCACTTGCGAGAGGACTCATCCTGTTTAGGCG -

- CGGGAGCGGATTTGAACGTTGCGAAGCAACGGCCCGGAGGGTGGCGGGCAGGACGCCCGC -
 - GCCCTCGCCTAAACTTGCAACGCTTCGTTGCCGGGCCTCCCACCGCCCGTCTTGCGGGCG -

- CATAAACTGCCAGGCATCAAATTAAGCAGAAGGCCATCCTGACGGATGGCCTTTTTCGCGT -
 - GTATTTGACGGTCCGTAGTTTAATTCGTCTTCCGGTAGGACTGCCTACCGGAAAAACGCA -

AatII

- TTCTACAAACTCTTTTGTATTATTTTCTAAATACATTCAAATATGGACGTCGTACTTAAC -
 - AAGATGTTTGAGAAAACAAATAAAAAGATTTATGTAAGTTTATACCTGCAGCATGAATTG -

- TTTTAAAGTATGGGCAATCAATTGCTCCTGTTAAATTGCTTTAGAAATACTTTGGCAGC -
 - AAAATTTTCATACCCGTTAGTTAACGAGGACAATTTTAACGAAATCTTTATGAAACCGTCG -

- GGTGTTGTTGATTGAGTTTCATTTGCGCATTGGTTAAATGGAAAGTGACCGTGCGCTTAC -
 - CCAAACAACATAACTCAAAGTAAACGCGTAACCAATTTACCTTTCCTGACGCGCAATG -

- TACAGCCTAATATTTTGAATATCCCAAGAGCTTTTTCCTTCGCATGCCACGCTAAAC -
 - ATGTCGGATTATAAAAACTTTATAGGGTCTCGAAAAAGGAAGCGTACGGGTGCGATTTG -

- ATTCTTTTCTCTTTTGGTTAAATCGTTGTTTGATTATTATTGCTATATTTATTTTTC -
 - TAAGAAAAAGAGAAAACCAATTTAGCAACAACTAAATAATAAACGATATAAATAAAAG -

- GATAATTATCAACTAGAGAAGGAACAATTAATGGTATGTTTCATACACGCATGTAAAAATA -
 - CTATTAATAGTTGATCTCTTCTTGTTAATTACCATAACAAGTATGTGCGTACATTTTAT -

- AACTATCTATATAGTTGTCTTCTCTGAATGTGCAAACTAAGCATTCCGAAGCCATTAT -
 - TTGATAGATATATCAACAGAAAGAGACTTACACGTTTGTATTGTAAGGCTTCGGTAATA -

- TAGCAGTATGAATAGGGAACTAAACCCAGTGATAAGACCTGATGATTTTCGCTTCTTAA -
 - ATCGTCATACTTATCCCTTTGATTGGGTCACTATTCTGGACTACTAAAGCGAAGAAATT -

- TTACATTTGGAGATTTTATTTACAGCATTGTTTCAAATATATTCCAATTAATCGGTG -
 - AATGTAAACCTCTAAAAATAAATGTCGTAACAAAAGTTTATATAAGGTTAATTAGCCAC -

- AATGATTGGAGTTAGAATAATCTACTATAGGATCATATTTTATTAAATTAGCGTCATCAT -
 - TTACTAACCTCAATCTTATTAGATGATATCCTAGTATAAAATAATTTAATCGCAGTAGTA -

- AATATTGCCTCCATTTTATAGGGTAATTATCCAGAATTGAAATATCAGATTTAACCATAG -
 - TTATAACGGAGGTAAAAAATCCCATTAATAGGTCTTAACCTTATAGTCTAAATTGGTATC -

- AATGAGGATAAATGATCGCGAGTAAATAATATTCACAAATGTACCATTTTAGTCATATCAG -
 - TTACTCCTATTTACTAGCGCTCATTTATTATAAGTGTTACATGGTAAATCAGTATAGTC -

- ATAAGCATTGATTAATATCATTATTGCTTCTACAGGCTTTAATTTTATTAATTATTCTGT -
 - TATTTCGTAACCTAATTATAGTAATAACGAAGATGTCCGAAATTAAAAATAATTAATAAGACA -

- AAGTGTCGTCGGCATTATGTCTTTCATACCCATCTCTTTATCCTTACCTATTGTTTGTG -
 - TTCACAGCAGCCGTAAATACAGAAAGTATGGGTAGAGAAATAGGAATGGATAACAAACAG -

- GCAAGTTTTGCGTGTTATATATCATTAAAAACGGTAATAGATTGACATTTGATTCTAATAA -
 - CGTTCAAACGCACAATATATAGTAATTTGCCATTATCTAACTGTAACTAAGATTATT -

FIG. 17B

- ATTGGATTTTGTGCACACTATTATATCGCTTGAAATACAATTGTTTAACATAAGTACCTG -
- TAACCTAAAAACAGTGTGATAATATAGCGAACTTTATGTTAACAAATTGTATTCATGGAC -
- TAGGATCGTACAGGTTTACGCAAGAAAATGGTTTGTATAGTCGATTAATCGATTTGATT -
- ATCCTAGCATGTCCAAATGCGTTCCTTTTACCAAACAATATCAGCTAATTAGCTAAACTAA -
- CTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGTTAACGCGTTGGAATTCGA -
- GATCTAAACAAAATTGATTAATTTCTCCTTATTGTATACCAATTGCGCAACCTTAAGCT -
- GCTCACTAGTGTCTGACCTGCAGGGTACCATGGAAGCTTACTCGAGGATCCGCGGAAAGAA -
- CGAGTGATCACAGCTGGACGTCCCATGGTACCTTCGAATGAGCTCCTAGGCGCCTTTCTT -
- GAAGAAGAAGAAGAAAGCCCGAAAGGAAGCTGAGTTGGCTGCTGCCACCGCTGAGCAATA -
- CTTCTTCTTCTTCTTTTCGGGCTTTCCTTCGACTCAACCGACGACGGTGGCGACTCGTTAT -
- ACTAGCATAACCCCTTGGGGCCTCTAAACGGGTCTTGAGGGGTTTTTTGCTGAAAGGAGG -
- TGATCGTATTGGGGAACCCCGGAGATTTGCCCAGAACTCCCCAAAAACGACTTTCCTCC -
- AACCGCTCTTCACGCTCTTCACGC 3' [SacII sticky end]
- TTGGCGAGAAGTGCGAGAAGTG 5' (position #5904 in pAMG21)

FIG.18A - 1

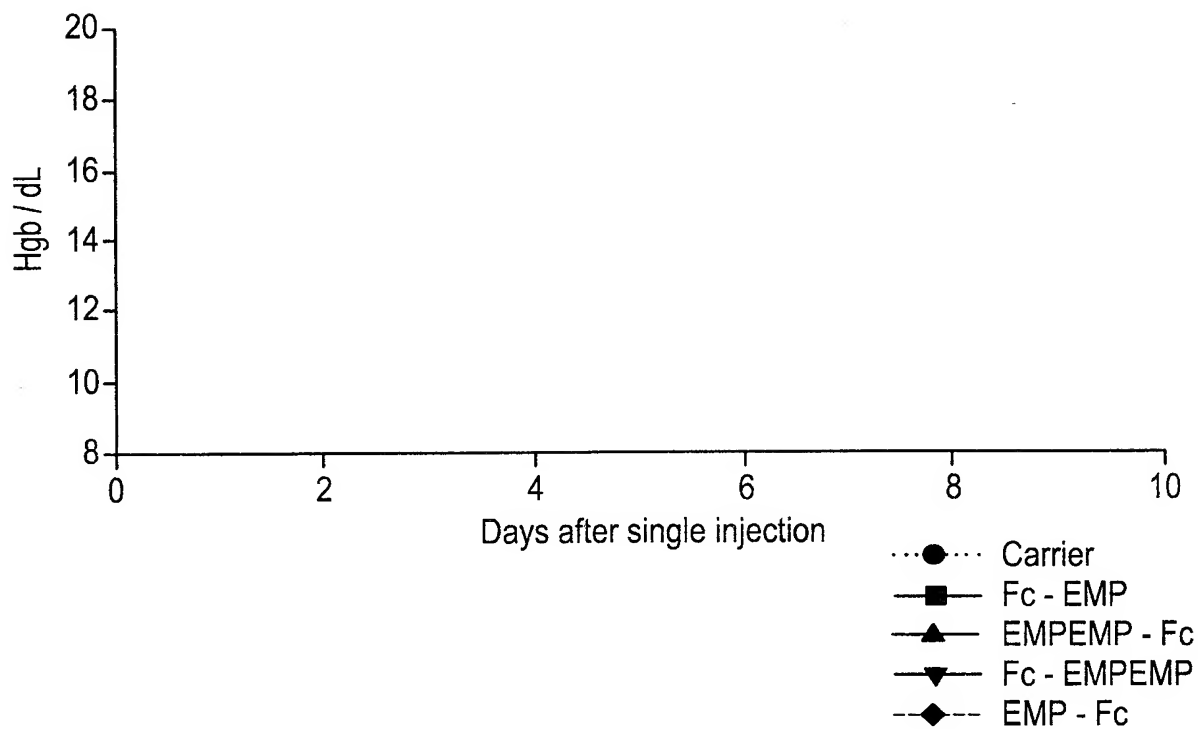


FIG.18A - 2

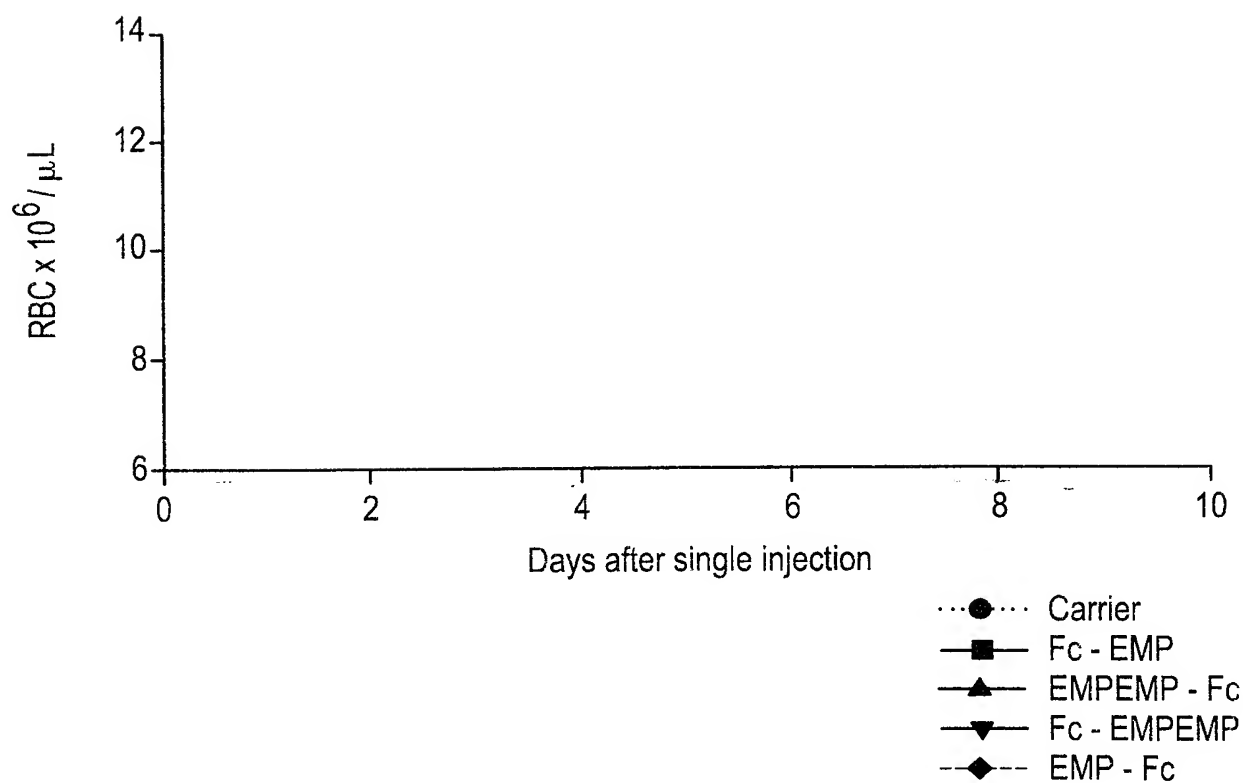


FIG.18A - 3

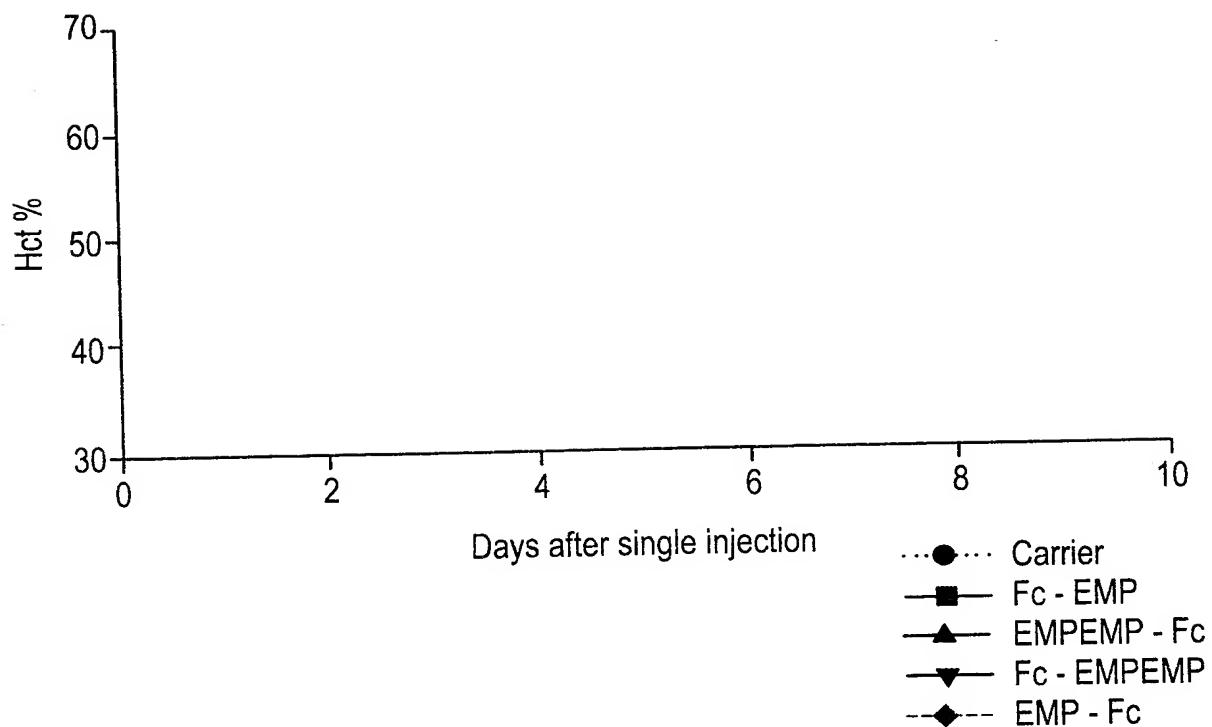


FIG.18B - 1

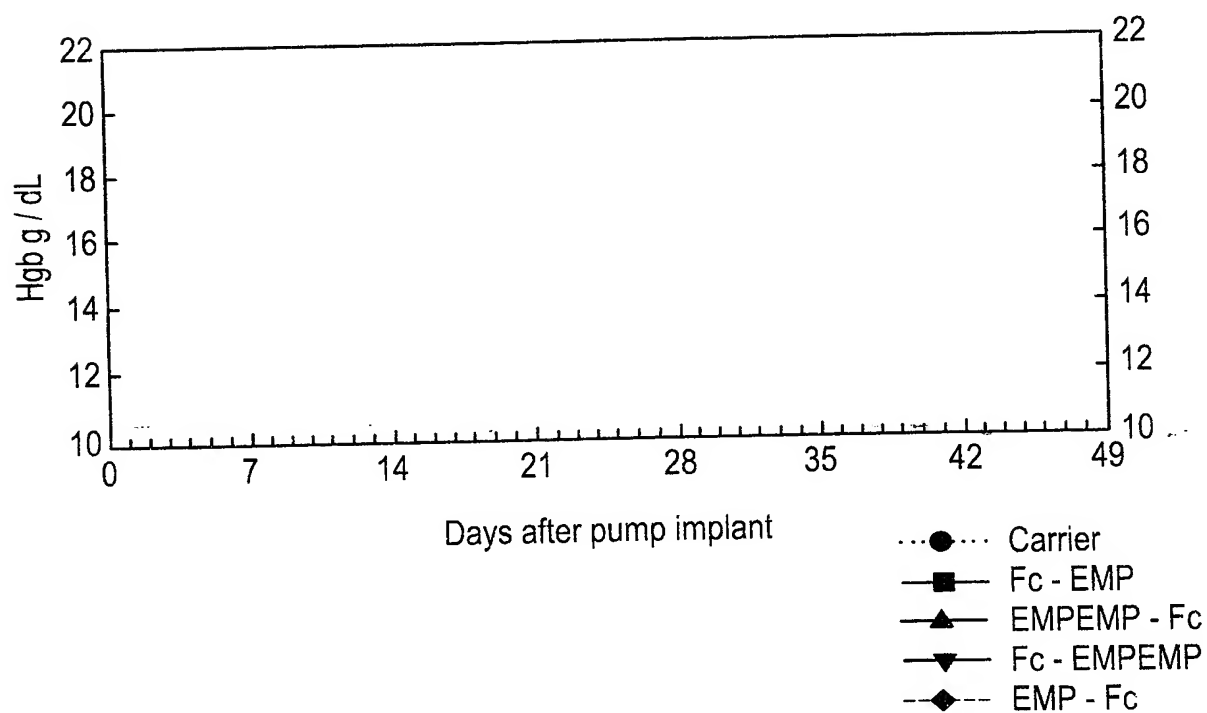


FIG.18B - 2

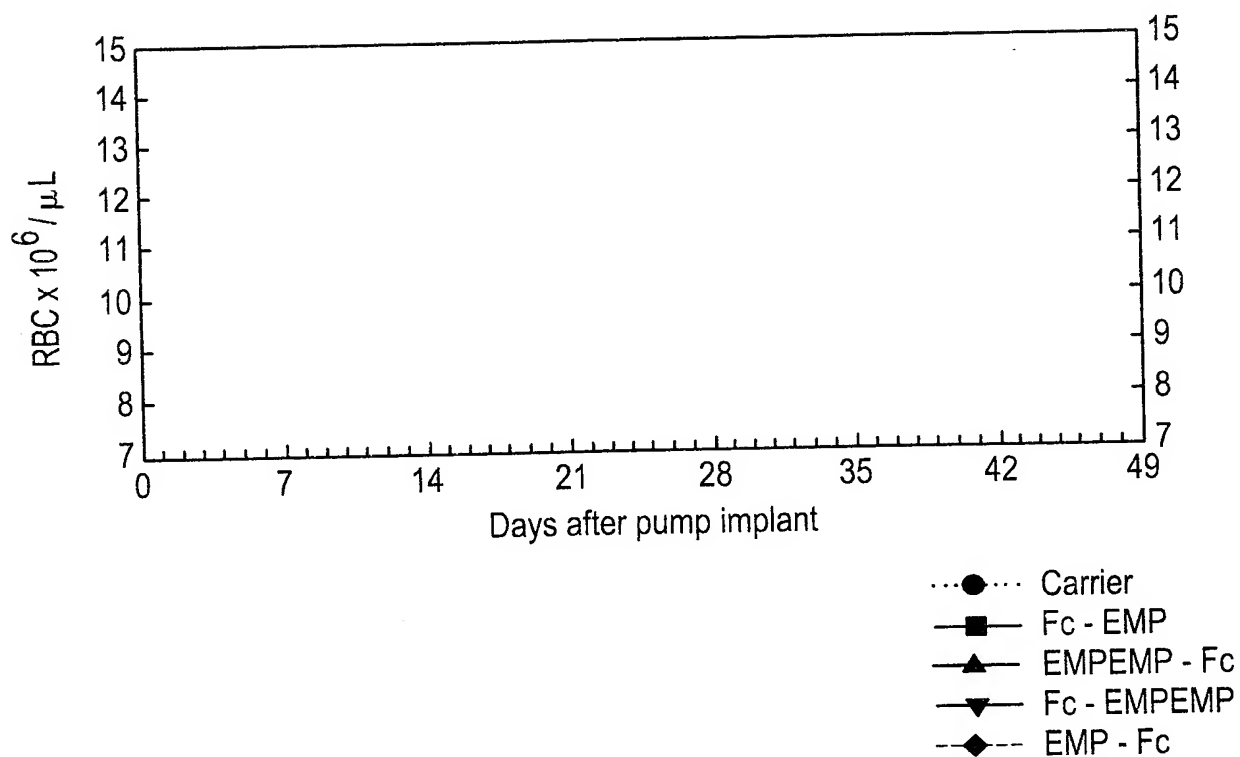


FIG.18B - 3

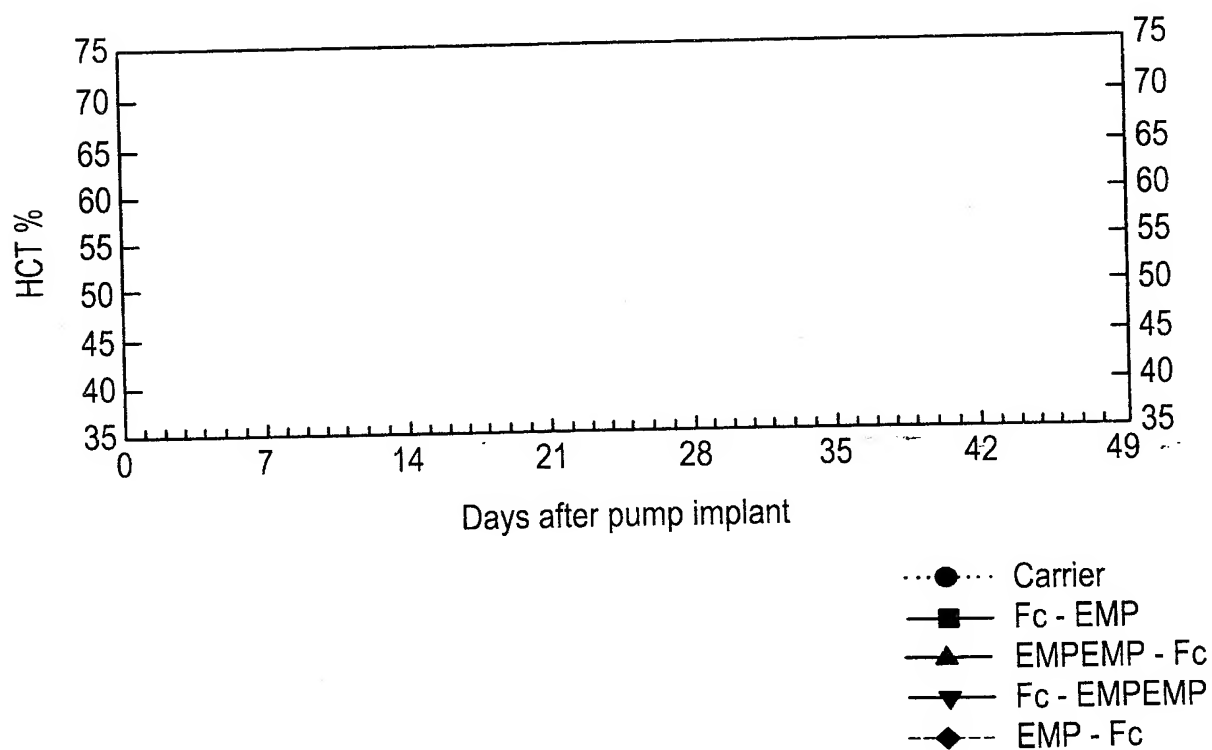


FIG. 19A

NdeI
|
1 CATATGGACAAAACCTCACACATGTCCACCTTGTCCAGCTCCGGAACCTCTGGGGGGACCG 60
-----+-----+-----+-----+-----+-----+
GTATACCTGTTTTGAGTGTGTACAGGTGGAACAGGTCGAGGCCTTGAGGACCCCCCTGGC
a M D K T H T C P P C P A P E L L G G P -
61 TCAGTCTTCTCTTCCCCCAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG 120
-----+-----+-----+-----+-----+-----+
AGTCAGAAGGAGAAGGGGGGTTTTGGGTTCTGTGGGAGTACTAGAGGGCCTGGGGACTC
a S V F L F P P K P K D T L M I S R T P E -
121 GTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTAC 180
-----+-----+-----+-----+-----+-----+
CAGTGTACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATG
a V T C V V V D V S H E D P E V K F N W Y -
181 GTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGC 240
-----+-----+-----+-----+-----+-----+
CACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCG
a V D G V E V H N A K T K P R E E Q Y N S -
241 ACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG 300
-----+-----+-----+-----+-----+-----+
TGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTTCCTC
a T Y R V V S V L T V L H Q D W L N G K E -
301 TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAA 360
-----+-----+-----+-----+-----+-----+
ATGTTACAGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTT
a Y K C K V S N K A L P A P I E K T I S K -
361 GCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG 420
-----+-----+-----+-----+-----+-----+
CGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGAC
a A K G Q P R E P Q V Y T L P P S R D E L -
421 ACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCC 480
-----+-----+-----+-----+-----+-----+
TGGTTCTTGGTCCAGTCGGAAGTGGACGGACAGTTTCCGAAGATAGGGTCGCTGTAGCGG
a T K N Q V S L T C L V K G F Y P S D I A -
481 GTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAAGACCACGCCTCCCGTGCTG 540
-----+-----+-----+-----+-----+-----+
CACCTCACCTCTCTCGTTACCCGTCGGCCTCTTGTGATGTTCTGGTGGGAGGGGCACGAC
a V E W E S N G Q P E N N Y K T T P P V L -
541 GACTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG 600
-----+-----+-----+-----+-----+-----+
CTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTTCGAGTGGCACCTGTTCTCGTCCACCGTC
a D S D G S F F L Y S K L T V D K S R W Q -

FIG. 19B

```

601 CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAG 660
-----+-----+-----+-----+-----+
a   Q G N V F S C S V M H E A L H N H Y T Q -
661 AAGAGCCTCTCCCTGTCTCCGGGTAAAGGTGGAGGTGGTGGTGA CTTCCCTGCCGCACTAC 720
-----+-----+-----+-----+-----+
a   K S L S L S P G K G G G G G D F L P H Y -
                                     BamHI
                                     |
721 AAAAACACCTCTCTGGGTCACCGTCCGTAATGGATCC 757
-----+-----+-----+-----+
a   K N T S L G H R P *
```

FIG. 20A

NdeI
|
1 CATATGGACTTCCTGCCGCACTACAAAAACACCTCTCTGGGTCACCGTCCGGGTGGAGGC 60
-----+-----+-----+-----+-----+-----+-----+
GTATACCTGAAGGACGGCGTGATGTTTTTGTGGAGAGACCCAGTGGCAGGCCACCTCCG
a M D F L P H Y K N T S L G H R P G G G -
61 GGTGGGGACAAAACCTCACACATGTCCACCTTGCCAGCACCTGAACTCCTGGGGGGACCG 120
-----+-----+-----+-----+-----+-----+-----+
CCACCCCTGTTTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCCCCTGGC
a G G D K T H T C P P C P A P E L L G G P -
121 TCAGTTTTCTCTTCCCCCAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG 180
-----+-----+-----+-----+-----+-----+-----+
AGTCAAAAGGAGAAGGGGGTTTTGGGTTCTGTGGGAGTACTAGAGGGCCTGGGGACTC
a S V F L F P P K P K D T L M I S R T P E -
181 GTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTAC 240
-----+-----+-----+-----+-----+-----+-----+
CAGTGTACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATG
a V T C V V V D V S H E D P E V K F N W Y -
241 GTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGC 300
-----+-----+-----+-----+-----+-----+-----+
CACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTGCG
a V D G V E V H N A K T K P R E E Q Y N S -
301 ACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG 360
-----+-----+-----+-----+-----+-----+-----+
TGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTTCTCTC
a T Y R V V S V L T V L H Q D W L N G K E -
361 TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCATCGAGAAAACCATCTCCAAC 420
-----+-----+-----+-----+-----+-----+-----+
ATGTTACAGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTT
a Y K C K V S N K A L P A P I E K T I S K -
421 GCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG 480
-----+-----+-----+-----+-----+-----+-----+
CGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGAC
a A K G Q P R E P Q V Y T L P P S R D E L -
481 ACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCC 540
-----+-----+-----+-----+-----+-----+-----+
TGGTTCTTGGTCCAGTCGGACTGGACGGACAGTTTCCGAAGATAGGGTCGCTGTAGCGG
a T K N Q V S L T C L V K G F Y P S D I A -
541 GTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAAGACCACGCCTCCCGTGCTG 600
-----+-----+-----+-----+-----+-----+-----+
CACCTCACCTCTCGTTACCCGTCGGCCTCTTGTGATGTTCTGGTGCGGAGGGGCACGAC
a V E W E S N G Q P E N N Y K T T P P V L -

FIG. 20B

601 GACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG 660
-----+-----+-----+-----+-----+-----+
CTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTTCGAGTGGCACCTGTTCTCGTCCACCGTC
a D S D G S F F L Y S K L T V D K S R W Q -
CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAG
661 -----+-----+-----+-----+-----+-----+ 720
GTCCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTC
a Q G N V F S C S V M H E A L H N H Y T Q -
BamHI
|
AAGAGCCTCTCCCTGTCTCCGGGTAAATAATGGATCCGCGG
721 -----+-----+-----+-----+-----+ 761
TTCTCGGAGAGGGACAGAGGCCCATTTATTACCTAGGCGCC
a K S L S L S P G K *

FIG. 21A

NdeI
|
CATATGGACAAAACCTCACACATGTCCACCTTGTCCAGCTCCGGAACCTCCTGGGGGGACCG
1 -----+-----+-----+-----+-----+-----+-----+ 60
GTATACCTGTTTTGAGTGTGTACAGGTGGAACAGGTCGAGGCCTTGAGGACCCCTGGC

a M D K T H T C P P C P A P E L L G G P -

TCAGTCTTCCTCTTCCCCCAAAACCAAGGACACCCTCATGATCTCCCGGACCCCTGAG
61 -----+-----+-----+-----+-----+-----+-----+ 120
AGTCAGAAGGAGAAGGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTC

a S V F L F P P K P K D T L M I S R T P E -

GTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTAC
121 -----+-----+-----+-----+-----+-----+-----+ 180
CAGTGACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATG

a V T C V V V D V S H E D P E V K F N W Y -

GTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGC
181 -----+-----+-----+-----+-----+-----+-----+ 240
CACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCTG

a V D G V E V H N A K T K P R E E Q Y N S -

ACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG
241 -----+-----+-----+-----+-----+-----+-----+ 300
TGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCTGACCGACTTACCGTTCCTC

a T Y R V V S V L T V L H Q D W L N G K E -

TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCATCGAGAAAACCATCTCCAAA
301 -----+-----+-----+-----+-----+-----+-----+ 360
ATGTTACAGTTCCAGAGGTTGTTTCGGGAGGGTTCGGGGGTAGCTCTTTTGGTAGAGGTTT

a Y K C K V S N K A L P A P I E K T I S K -

GCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG
361 -----+-----+-----+-----+-----+-----+-----+ 420
CGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGAC

a A K G Q P R E P Q V Y T L P P S R D E L -

ACCAAGAACCAGGTGAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCC
421 -----+-----+-----+-----+-----+-----+-----+ 480
TGGTTCTTGGTCCAGTCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGG

a T K N Q V S L T C L V K G F Y P S D I A -

GTGGAGTGGGAGAGCAATGGGCAGCCGGAACAACACTACAAGACCACGCCTCCCGTGTCTG
481 -----+-----+-----+-----+-----+-----+-----+ 540
CACCTCACCTCTCGTTACCCGTCGGCCTCTTGTGATGTTCTGGTGGGAGGGCAGCAG

a V E W E S N G Q P E N N Y K T T P P V L -

GACTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG
541 -----+-----+-----+-----+-----+-----+-----+ 600
CTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTTCGAGTGGCACCTGTTCTCGTCCACCGTC

a D S D G S F F L Y S K L T V D K S R W Q -

FIG. 21B

601 CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAG 660
-----+-----+-----+-----+-----+-----+
GTCCCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTC
a Q G N V F S C S V M H E A L H N H Y T Q -
AAGAGCCTCTCCCTGTCTCCGGGTAAAGGTGGAGGTGGTGGTTTCGAATGGACCCCGGGT
661 -----+-----+-----+-----+-----+-----+ 720
TTCTCGGAGAGGGACAGAGGCCCATTTCCACCTCCACCACCAAAGCTTACCTGGGGCCCA
a K S L S L S P G K G G G G G F E W T P G -
BamHI
|
TACTGGCAGCCGTACGCTCTGCCGCTGTAATGGATCCCTCGAG
721 -----+-----+-----+-----+-----+ 763
ATGACCGTCGGCATGCGAGACGGCGACATTACCTAGGGAGCTC
a Y W Q P Y A L P L *

FIG. 22A

NdeI
|
CATATGTTTCGAATGGACCCCGGGTTACTGGCAGCCGTACGCTCTGCCGCTGGGTGGAGGC
1 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 60
GTATACAAGCTTACCTGGGGCCCAATGACCGTCGGCATGCGAGACGGCGACCCACCTCCG
a M F E W T P G Y W Q P Y A L P L G G G -
GGTGGGGACAAAACCTCACACATGTCCACCTTGCCCAGCACCTGAACTCCTGGGGGGACCG
61 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 120
CCACCCCTGTTTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCCTGGC
a G G D K T H T C P P C P A P E L L G G P -
TCAGTTTTCTCTTCCCCCAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG
121 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 180
AGTCAAAAGGAGAAGGGGGGTTTTGGGTTCTGTGGGAGTACTAGAGGGCCTGGGGACTC
a S V F L F P P K P K D T L M I S R T P E -
GTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTAC
181 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 240
CAGTGTACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATG
a V T C V V V D V S H E D P E V K F N W Y -
GTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGC
241 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 300
CACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTGC
a V D G V E V H N A K T K P R E E Q Y N S -
ACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG
301 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 360
TGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCTGACCGACTTACCGTTCCTC
a T Y R V V S V L T V L H Q D W L N G K E -
TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCATCGAGAAAACCATCTCCAAA
361 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 420
ATGTTACAGTTCCAGAGGTTGTTTCGGGAGGGTGGGGGTAGCTCTTTTGGTAGAGGTTT
a Y K C K V S N K A L P A P I E K T I S K -
GCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG
421 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 480
CGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGAC
a A K G Q P R E P Q V Y T L P P S R D E L -
ACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCC
481 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 540
TGGTCTTGGTCCAGTCGGACTGGACGGACAGTTTCCGAAGATAGGGTCGCTGTAGCGG
a T K N Q V S L T C L V K G F Y P S D I A -
GTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAAGACCACGCCTCCCGTGCTG
541 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 600
CACCTACCCCTCTCGTTACCCGTCGGCCTCTTGTGATGTTCTGGTGCAGGAGGCACGAC
a V E W E S N G Q P E N N Y K T T P P V L -

FIG. 22B

```

601 GACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG
-----+-----+-----+-----+-----+-----+-----+ 660
CTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTTCGAGTGGCACCTGTTCTCGTCCACCGTC

a   D S D G S F F L Y S K L T V D K S R W Q -

661 CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAG
-----+-----+-----+-----+-----+-----+ 720
GTCCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTC

a   Q G N V F S C S V M H E A L H N H Y T Q -

                                     BamHI
                                     |
721 AAGAGCCTCTCCCTGTCTCCGGGTAAATAATGGATCC
-----+-----+-----+-----+-----+ 757
TTCTCGGAGAGGGACAGAGGCCCATTTATTACCTAGG

a   K S L S L S P G K *
```

FIG. 23A

NdeI
|
CATATGGACAAACTCACACATGTCCACCGTGCCAGCACCTGAACTCCTGGGGGGACCG
1 -----+-----+-----+-----+-----+-----+-----+ 60
GTATACCTGTTTTGAGTGTGTACAGGTGGCACGGGTCGTGGACTTGAGGACCCCCCTGGC

a M D K T H T C P P C P A P E L L G G P -

61 TCAGTTTTCTCTTCCCCCAAAACCAAGGACACCCTCATGATCTCCCGGACCCCTGAG
-----+-----+-----+-----+-----+-----+-----+ 120
AGTCAAAGGAGAAGGGGGGTTTTGGGTTCTGTGGGAGTACTAGAGGGCCTGGGGACTC

a S V F L F P P K P K D T L M I S R T P E -

121 GTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTAC
-----+-----+-----+-----+-----+-----+-----+ 180
CAGTGACGCACACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATG

a V T C V V V D V S H E D P E V K F N W Y -

181 GTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGC
-----+-----+-----+-----+-----+-----+-----+ 240
CACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCG

a V D G V E V H N A K T K P R E E Q Y N S -

241 ACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG
-----+-----+-----+-----+-----+-----+-----+ 300
TGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTTCTC

a T Y R V V S V L T V L H Q D W L N G K E -

301 TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCATCGAGAAAACCATCTCCAA
-----+-----+-----+-----+-----+-----+-----+ 360
ATGTTACAGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTGGTAGAGGTTT

a Y K C K V S N K A L P A P I E K T I S K -

361 GCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG
-----+-----+-----+-----+-----+-----+-----+ 420
CGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGAC

a A K G Q P R E P Q V Y T L P P S R D E L -

421 ACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCC
-----+-----+-----+-----+-----+-----+-----+ 480
TGGTTCTTGGTCCAGTCGGACTGGACGGACCAGTTCCGAAGATAGGGTCGCTGTAGCGG

a T K N Q V S L T C L V K G F Y P S D I A -

481 GTGGAGTGGGAGAGCAATGGGCAGCCGGAACAACACTACAAGACCACGCCTCCCGTGCTG
-----+-----+-----+-----+-----+-----+-----+ 540
CACCTCACCTCTCGTTACCCGTCGGCCTCTTGTGATGTTCTGGTGGGAGGGGCACGAC

a V E W E S N G Q P E N N Y K T T P P V L -

541 GACTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG
-----+-----+-----+-----+-----+-----+-----+ 600
CTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTTCGAGTGGCACCTGTTCTCGTCCACCGTC

a D S D G S F F L Y S K L T V D K S R W Q -

FIG. 23B

[illegible]

FIG. 24A

NdeI
|
CATATGGTTGAACCGAACTGTGACATCCATGTTATGTGGGAATGGGAATGTTTTGAACGT
1 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 60
GTATACCAACTTGGCTTGACACTGTAGGTACAATACACCCTTACCCTTACAAAACCTTGCA
a M V E P N C D I H V M W E W E C F E R -
CTGGGTGGTGGTGGTGGTGACAAACTCACACATGTCCACCGTGCCAGCACCTGAACTC
61 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 120
GACCCACCACCACCACCCTGTTTTGAGTGTGTACAGGTGGCACGGGTCGTGGACTTGAG
a L G G G G G D K T H T C P P C P A P E L -
CTGGGGGGACCGTCAGTTTTCTCTTCCCCCAAAACCAAGGACACCCCTCATGATCTCC
121 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 180
GACCCCCCTGGCAGTCAAAGGAGAAGGGGGGTTTTGGGTTCTGTGGGAGTACTAGAGG
a L G G P S V F L F P P K P K D T L M I S -
CGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCCTGAGGTCAAG
181 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 240
GCCTGGGGACTCCAGTGTACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTC
a R T P E V T C V V V D V S H E D P E V K -
TTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAG
241 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 300
AAGTTGACCATGCACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTC
a F N W Y V D G V E V H N A K T K P R E E -
CAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTG
301 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 360
GTCATGTTGTCGTGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGAC
a Q Y N S T Y R V V S V L T V L H Q D W L -
AATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAA
361 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 420
TTACCGTTCCTCATGTTTCAGTTCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTT
a N G K E Y K C K V S N K A L P A P I E K -
ACCATCTCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCCTGCCCCCATCC
421 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 480
TGGTAGAGGTTTCGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGG
a T I S K A K G Q P R E P Q V Y T L P P S -
CGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCC
481 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 540
GCCCTACTCGACTGGTTCCTTGGTCCAGTCGGACTGGACGGACAGTTTCCGAAGATAGGG
a R D E L T K N Q V S L T C L V K G F Y P -
AGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACCTACAAGACCACG
541 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 600
TCGCTGTAGCGGCACCTCACCCCTCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTG
a S D I A V E W E S N G Q P E N N Y K T T -

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FIG. 24B

```

601 CCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAG 660
    -----+-----+-----+-----+-----+-----+
    GGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTTCGAGTGGCACCTGTTC
a      P P V L D S D G S F F L Y S K L T V D K -

661 AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAAC 720
    -----+-----+-----+-----+-----+-----+
    TCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTG
a      S R W Q Q G N V F S C S V M H E A L H N -

                                           BamHI
                                           |
721 CACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATAACTCGAGGATCC 773
    -----+-----+-----+-----+-----+-----+
    GTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCATTTATTGAGCTCCTAGG
a      H Y T Q K S L S L S P G K *
```

FIG. 25A

NdeI
|
CATATGGACAAAACTCACACATGTCCACCTTGTCCAGCTCCGGAACCTCTGGGGGGACCG
1 -----+-----+-----+-----+-----+-----+-----+ 60
GTATACCTGTTTTGAGTGTGTACAGGTGGAACAGGTCGAGGCCTTGAGGACCCCCCTGGC

a M D K T H T C P P C P A P E L L G G P -

TCAGTCTTCCTCTTCCCCCAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG
61 -----+-----+-----+-----+-----+-----+-----+ 120
AGTCAGAAGGAGAAGGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGCCTGGGGACTC

a S V F L F P P K P K D T L M I S R T P E -

GTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTAC
121 -----+-----+-----+-----+-----+-----+-----+ 180
CAGTGACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATG

a V T C V V V D V S H E D P E V K F N W Y -

GTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGC
181 -----+-----+-----+-----+-----+-----+-----+ 240
CACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCG

a V D G V E V H N A K T K P R E E Q Y N S -

ACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG
241 -----+-----+-----+-----+-----+-----+-----+ 300
TGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCTCTGACCGACTTACCGTTCCTC

a T Y R V V S V L T V L H Q D W L N G K E -

TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCATCGAGAAAACCATCTCCAAA
301 -----+-----+-----+-----+-----+-----+-----+ 360
ATGTTACAGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTT

a Y K C K V S N K A L P A P I E K T I S K -

GCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG
361 -----+-----+-----+-----+-----+-----+-----+ 420
CGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGAC

a A K G Q P R E P Q V Y T L P P S R D E L -

ACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCC
421 -----+-----+-----+-----+-----+-----+-----+ 480
TGGTTCTTGGTCCAGTCGGAAGTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGG

a T K N Q V S L T C L V K G F Y P S D I A -

GTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACCTACAAGACCACGCCTCCCGTGCTG
481 -----+-----+-----+-----+-----+-----+-----+ 540
CACCTCACCTCTCGTTACCCGTCGGCCTCTTGTGATGTTCTGGTGGGAGGGGCACGAC

a V E W E S N G Q P E N N Y K T T P P V L -

GACTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG
541 -----+-----+-----+-----+-----+-----+-----+ 600
CTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTTCGAGTGGCACCTGTTCTCGTCCACCGTC

a D S D G S F F L Y S K L T V D K S R W Q -

FIG. 25B

```
601 CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAG 660
-----+-----+-----+-----+-----+-----+
a   GTCCCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTC

    Q G N V F S C S V M H E A L H N H Y T Q -
    AAGAGCCTCTCCCTGTCTCCGGGTAAAGGTGGAGGTGGTGGTTGCACCACCACTGGGGT
661 -----+-----+-----+-----+-----+ 720
    TTCTCGGAGAGGGACAGAGGCCCATTTCCACCTCCACCACCAACGTGGTGGGTGACCCCA

A   K S L S L S P G K G G G G G C T T H W G -

          BamHI
          |
    TTCACCCTGTGCTAATGGATCCCTCGAG
721 -----+-----+-----+-----+ 748
    AAGTGGGACACGATTACCTAGGGAGCTC

a   F T L C *
```

FIG. 26A

NdeI
|
CATATGTGCACCACCCACTGGGGTTTCACCCTGTGCGGTGGAGGCGGTGGGGACAAAGGT
1 -----+-----+-----+-----+-----+-----+ 60
GTATACACGTGGTGGGTGACCCCAAAGTGGGACACGCCACCTCCGCCACCCCTGTTTCCA
a M C T T H W G F T L C G G G G G D K G -
GGAGGCGGTGGGGACAAACTCACACATGTCCACCTTGCCCAGCACCTGAACTCCTGGGG
61 -----+-----+-----+-----+-----+-----+ 120
CCTCCGCCACCCCTGTTTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCC
a G G G G D K T H T C P P C P A P E L L G -
GGACCGTCAGTTTTCTCTCCCCCAAACCCAAGGACACCCTCATGATCTCCCGGACC
121 -----+-----+-----+-----+-----+-----+ 180
CCTGGCAGTCAAAAGGAGAAGGGGGTTTTGGGTTCTGTGGGAGTACTAGAGGGCCTGG
a G P S V F L F P P K P K D T L M I S R T -
CCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAAC
181 -----+-----+-----+-----+-----+-----+ 240
GGACTCCAGTGTACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTG
a P E V T C V V V D V S H E D P E V K F N -
TGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTAC
241 -----+-----+-----+-----+-----+-----+ 300
ACCATGCACCTGCCGCACCTCCACGTATTACGGTTCTGTTCGGGCGCCCTCCTCGTCATG
a W Y V D G V E V H N A K T K P R E E Q Y -
AACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGC
301 -----+-----+-----+-----+-----+-----+ 360
TTGTCGTGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCG
a N S T Y R V V S V L T V L H Q D W L N G -
AAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATC
361 -----+-----+-----+-----+-----+-----+ 420
TTCCTCATGTTACGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAG
a K E Y K C K V S N K A L P A P I E K T I -
TCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGAT
421 -----+-----+-----+-----+-----+-----+ 480
AGGTTTCGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGTAGGGCCCTA
a S K A K G Q P R E P Q V Y T L P P S R D -
GAGCTGACCAAGAACCAGGTGAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGAC
481 -----+-----+-----+-----+-----+-----+ 540
CTCGACTGGTTCTTGGTCCAGTCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTG
a E L T K N Q V S L T C L V K G F Y P S D -
ATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAAGACCACGCCCTCC
541 -----+-----+-----+-----+-----+-----+ 600
TAGCGGCACCTCACCTCTCGTTACCCGTCGGCCTCTTGTGATGTTCTGGTGGGAGGG
a I A V E W E S N G Q P E N N Y K T T P P -

FIG. 26B

```

601  GTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGG 660
      -----+-----+-----+-----+-----+-----+
      CACGACCTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTTCGAGTGGCACCTGTTCTCGTCC
a    V  L  D  S  D  G  S  F  F  L  Y  S  K  L  T  V  D  K  S  R  -

      TGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC
661  -----+-----+-----+-----+-----+-----+ 720
      ACCGTCGTCCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATG
a    W  Q  Q  G  N  V  F  S  C  S  V  M  H  E  A  L  H  N  H  Y  -

                                     BamHI
                                     |
      ACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATAATGGATCC
721  -----+-----+-----+-----+-----+ 763
      TCGTCTTCTCGGAGAGGGACAGAGGCCCATTTATTACCTAGG
a    T  Q  K  S  L  S  L  S  P  G  K  *
```

SEQUENCE LISTING

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<120> MODIFIED PEPTIDES AS THERAPEUTIC AGENTS

<130> A-527

<140> NOT YET RECEIVED

<141> 1999-10-22

<150> 60/105,371

<151> 1998-10-23

<160> 1133

<170> PatentIn Ver. 2.1

<210> 1

<211> 684

<212> DNA

<213> HUMAN

<220>

<221> CDS

<222> (1)..(684)

<400> 1

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| atg | gac | aaa | act | cac | aca | tgt | cca | cct | tgt | cca | gct | ccg | gaa | ctc | ctg | 48 |
| Met | Asp | Lys | Thr | His | Thr | Cys | Pro | Pro | Cys | Pro | Ala | Pro | Glu | Leu | Leu | |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| ggg | gga | ccg | tca | gtc | ttc | ctc | ttc | ccc | cca | aaa | ccc | aag | gac | acc | ctc | 96 |
| Gly | Gly | Pro | Ser | Val | Phe | Leu | Phe | Pro | Pro | Lys | Pro | Lys | Asp | Thr | Leu | |
| | | | 20 | | | | | 25 | | | | | 30 | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| atg | atc | tcc | cgg | acc | cct | gag | gtc | aca | tgc | gtg | gtg | gtg | gac | gtg | agc | 144 |
| Met | Ile | Ser | Arg | Thr | Pro | Glu | Val | Thr | Cys | Val | Val | Val | Asp | Val | Ser | |
| | | 35 | | | | | 40 | | | | | 45 | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| cac | gaa | gac | cct | gag | gtc | aag | ttc | aac | tgg | tac | gtg | gac | ggc | gtg | gag | 192 |
| His | Glu | Asp | Pro | Glu | Val | Lys | Phe | Asn | Trp | Tyr | Val | Asp | Gly | Val | Glu | |
| | 50 | | | | | | 55 | | | | 60 | | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| gtg | cat | aat | gcc | aag | aca | aag | ccg | cgg | gag | gag | cag | tac | aac | agc | acg | 240 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Val | His | Asn | Ala | Lys | Thr | Lys | Pro | Arg | Glu | Glu | Gln | Tyr | Asn | Ser | Thr | | |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 | | |
| tac | cgt | gtg | gtc | agc | gtc | ctc | acc | gtc | ctg | cac | cag | gac | tgg | ctg | aat | 288 | |
| Tyr | Arg | Val | Val | Ser | Val | Leu | Thr | Val | Leu | His | Gln | Asp | Trp | Leu | Asn | | |
| | | | | 85 | | | | | 90 | | | | | 95 | | | |
| ggc | aag | gag | tac | aag | tgc | aag | gtc | tcc | aac | aaa | gcc | ctc | cca | gcc | ccc | 336 | |
| Gly | Lys | Glu | Tyr | Lys | Cys | Lys | Val | Ser | Asn | Lys | Ala | Leu | Pro | Ala | Pro | | |
| | | | 100 | | | | | 105 | | | | | 110 | | | | |
| atc | gag | aaa | acc | atc | tcc | aaa | gcc | aaa | ggg | cag | ccc | cga | gaa | cca | cag | 384 | |
| Ile | Glu | Lys | Thr | Ile | Ser | Lys | Ala | Lys | Gly | Gln | Pro | Arg | Glu | Pro | Gln | | |
| | | 115 | | | | | 120 | | | | | 125 | | | | | |
| gtg | tac | acc | ctg | ccc | cca | tcc | cgg | gat | gag | ctg | acc | aag | aac | cag | gtc | 432 | |
| Val | Tyr | Thr | Leu | Pro | Pro | Ser | Arg | Asp | Glu | Leu | Thr | Lys | Asn | Gln | Val | | |
| | 130 | | | | | 135 | | | | | 140 | | | | | | |
| agc | ctg | acc | tgc | ctg | gtc | aaa | ggc | ttc | tat | ccc | agc | gac | atc | gcc | gtg | 480 | |
| Ser | Leu | Thr | Cys | Leu | Val | Lys | Gly | Phe | Tyr | Pro | Ser | Asp | Ile | Ala | Val | | |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 | | |
| gag | tgg | gag | agc | aat | ggg | cag | ccg | gag | aac | aac | tac | aag | acc | acg | cct | 528 | |
| Glu | Trp | Glu | Ser | Asn | Gly | Gln | Pro | Glu | Asn | Asn | Tyr | Lys | Thr | Thr | Pro | | |
| | | | | 165 | | | | | 170 | | | | | 175 | | | |
| ccc | gtg | ctg | gac | tcc | gac | ggc | tcc | ttc | ttc | ctc | tac | agc | aag | ctc | acc | 576 | |
| Pro | Val | Leu | Asp | Ser | Asp | Gly | Ser | Phe | Phe | Leu | Tyr | Ser | Lys | Leu | Thr | | |
| | | | 180 | | | | | 185 | | | | | | 190 | | | |
| gtg | gac | aag | agc | agg | tgg | cag | cag | ggg | aac | gtc | ttc | tca | tgc | tcc | gtg | 624 | |
| Val | Asp | Lys | Ser | Arg | Trp | Gln | Gln | Gly | Asn | Val | Phe | Ser | Cys | Ser | Val | | |
| | | 195 | | | | | 200 | | | | | 205 | | | | | |
| atg | cat | gag | gct | ctg | cac | aac | cac | tac | acg | cag | aag | agc | ctc | tcc | ctg | 672 | |
| Met | His | Glu | Ala | Leu | His | Asn | His | Tyr | Thr | Gln | Lys | Ser | Leu | Ser | Leu | | |
| | | 210 | | | | 215 | | | | | 220 | | | | | | |
| tct | ccg | ggt | aaa | | | | | | | | | | | | | 684 | |
| Ser | Pro | Gly | Lys | | | | | | | | | | | | | | |
| 225 | | | | | | | | | | | | | | | | | |

<210> 2

<211> 228

<212> PRT

<213> HUMAN

<400> 2

```

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
  1              5              10              15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
      20              25              30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
      35              40              45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
      50              55              60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
      65              70              75              80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
      85              90              95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
      100              105              110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
      115              120              125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
      130              135              140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
      145              150              155              160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
      165              170              175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
      180              185              190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
      195              200              205

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
      210              215              220

Ser Pro Gly Lys
      225

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<210> 3
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PEGYLATED
PEPTIDE

<400> 3
Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala
1 5 10 15

Arg Ala

<210> 4
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PEGYLATED
PEPTIDE

<400> 4
Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala
1 5 10 15

Arg Ala

<210> 5
<211> 794
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Fc-TMP

<220>
<221> CDS
<222> (39) .. (779)

<400> 5

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tctagatttg ttttaactaa ttaaaggagg aataacat atg gac aaa act cac aca 56
                               Met Asp Lys Thr His Thr
                               1               5

tgt cca cct tgt cca gct ccg gaa ctc ctg ggg gga ccg tca gtc ttc 104
Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
          10               15               20

ctc ttc ccc cca aaa ccc aag gac acc ctc atg atc tcc cgg acc cct 152
Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
          25               30               35

gag gtc aca tgc gtg gtg gtg gac gtg agc cac gaa gac cct gag gtc 200
Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
          40               45               50

aag ttc aac tgg tac gtg gac ggc gtg gag gtg cat aat gcc aag aca 248
Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
          55               60               65               70

aag ccg cgg gag gag cag tac aac agc acg tac cgt gtg gtc agc gtc 296
Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
          75               80               85

ctc acc gtc ctg cac cag gac tgg ctg aat ggc aag gag tac aag tgc 344
Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
          90               95               100

aag gtc tcc aac aaa gcc ctc cca gcc ccc atc gag aaa acc atc tcc 392
Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
          105               110               115

aaa gcc aaa ggg cag ccc cga gaa cca cag gtg tac acc ctg ccc cca 440
Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
          120               125               130

tcc cgg gat gag ctg acc aag aac cag gtc agc ctg acc tgc ctg gtc 488
Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
          135               140               145               150

aaa ggc ttc tat ccc agc gac atc gcc gtg gag tgg gag agc aat ggg 536
Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
          155               160               165

cag ccg gag aac aac tac aag acc acg cct ccc gtg ctg gac tcc gac 584
Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp

```


| 170 | 175 | 180 | |
|---|-----|-----|-----|
| ggc tcc ttc ttc ctc tac agc aag ctc acc gtg gac aag agc agg tgg | | | 632 |
| Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp | | | |
| 185 | 190 | 195 | |
| cag cag ggg aac gtc ttc tca tgc tcc gtg atg cat gag gct ctg cac | | | 680 |
| Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His | | | |
| 200 | 205 | 210 | |
| aac cac tac acg cag aag agc ctc tcc ctg tct ccg ggt aaa ggt gga | | | 728 |
| Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly | | | |
| 215 | 220 | 225 | 230 |
| ggt ggt ggt atc gaa ggt ccg act ctg cgt cag tgg ctg gct gct cgt | | | 776 |
| Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg | | | |
| 235 | 240 | 245 | |
| gct taatctcgag gatcc | | | 794 |
| Ala | | | |

<210> 6

<211> 247

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc-TMP

<400> 6

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Asp | Lys | Thr | His | Thr | Cys | Pro | Pro | Cys | Pro | Ala | Pro | Glu | Leu | Leu |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Gly | Pro | Ser | Val | Phe | Leu | Phe | Pro | Pro | Lys | Pro | Lys | Asp | Thr | Leu |
| | | | 20 | | | | | 25 | | | | | 30 | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ile | Ser | Arg | Thr | Pro | Glu | Val | Thr | Cys | Val | Val | Val | Asp | Val | Ser |
| | | 35 | | | | | 40 | | | | 45 | | | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| His | Glu | Asp | Pro | Glu | Val | Lys | Phe | Asn | Trp | Tyr | Val | Asp | Gly | Val | Glu |
| | 50 | | | | | 55 | | | | | 60 | | | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | His | Asn | Ala | Lys | Thr | Lys | Pro | Arg | Glu | Glu | Gln | Tyr | Asn | Ser | Thr |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Tyr | Arg | Val | Val | Ser | Val | Leu | Thr | Val | Leu | His | Gln | Asp | Trp | Leu | Asn |
| | | | | 85 | | | | | 90 | | | | | 95 | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Lys | Glu | Tyr | Lys | Cys | Lys | Val | Ser | Asn | Lys | Ala | Leu | Pro | Ala | Pro |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|

| | | |
|---|-----|-----|
| 100 | 105 | 110 |
| Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln | | |
| 115 | 120 | 125 |
| Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val | | |
| 130 | 135 | 140 |
| Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val | | |
| 145 | 150 | 155 |
| Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro | | |
| 165 | 170 | 175 |
| Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr | | |
| 180 | 185 | 190 |
| Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val | | |
| 195 | 200 | 205 |
| Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu | | |
| 210 | 215 | 220 |
| Ser Pro Gly Lys Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg | | |
| 225 | 230 | 235 |
| Gln Trp Leu Ala Ala Arg Ala | | |
| 245 | | |

<210> 7
 <211> 861
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:Fc-TMP-TMP

<220>
 <221> CDS
 <222> (39)..(842)

<400> 7
 tctagatttg ttttaactaa ttaaaggagg aataacat atg gac aaa act cac aca 56
 Met Asp Lys Thr His Thr
 1 5

| | |
|---|-----|
| tgt cca cct tgt cca gct ccg gaa ctc ctg ggg gga ccg tca gtc ttc | 104 |
| Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe | |
| 10 15 20 | |
| ctc ttc ccc cca aaa ccc aag gac acc ctc atg atc tcc cgg acc cct | 152 |
| Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro | |
| 25 30 35 | |
| gag gtc aca tgc gtg gtg gtg gac gtg agc cac gaa gac cct gag gtc | 200 |
| Glu Val Thr Cys Val Val Val Val Asp Val Ser His Glu Asp Pro Glu Val | |
| 40 45 50 | |
| aag ttc aac tgg tac gtg gac ggc gtg gag gtg cat aat gcc aag aca | 248 |
| Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr | |
| 55 60 65 70 | |
| aag ccg cgg gag gag cag tac aac agc acg tac cgt gtg gtc agc gtc | 296 |
| Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val | |
| 75 80 85 | |
| ctc acc gtc ctg cac cag gac tgg ctg aat ggc aag gag tac aag tgc | 344 |
| Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys | |
| 90 95 100 | |
| aag gtc tcc aac aaa gcc ctc cca gcc ccc atc gag aaa acc atc tcc | 392 |
| Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser | |
| 105 110 115 | |
| aaa gcc aaa ggg cag ccc cga gaa cca cag gtg tac acc ctg ccc cca | 440 |
| Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro | |
| 120 125 130 | |
| tcc cgg gat gag ctg acc aag aac cag gtc agc ctg acc tgc ctg gtc | 488 |
| Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val | |
| 135 140 145 150 | |
| aaa ggc ttc tat ccc agc gac atc gcc gtg gag tgg gag agc aat ggg | 536 |
| Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly | |
| 155 160 165 | |
| cag ccg gag aac aac tac aag acc acg cct ccc gtg ctg gac tcc gac | 584 |
| Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp | |
| 170 175 180 | |
| ggc tcc ttc ttc ctc tac agc aag ctc acc gtg gac aag agc agg tgg | 632 |
| Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp | |
| 185 190 195 | |

cag cag ggg aac gtc ttc tca tgc tcc gtg atg cat gag gct ctg cac 680
 Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
 200 205 210

aac cac tac acg cag aag agc ctc tcc ctg tct ccg ggt aaa ggt gga 728
 Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly
 215 220 225 230

ggt ggt ggt atc gaa ggt ccg act ctg cgt cag tgg ctg gct gct cgt 776
 Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg
 235 240 245

gct ggt ggt gga ggt ggc ggc gga ggt att gag ggc cca acc ctt cgc 824
 Ala Gly Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg
 250 255 260

caa tgg ctt gca gca cgc gcataatctc gaggatccg 861
 Gln Trp Leu Ala Ala Arg
 265

<210> 8

<211> 268

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc-TMP-TMP

<400> 8

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
 1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
 20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
 65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
 85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
 100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
 115 120 125
 Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
 130 135 140
 Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
 145 150 155 160
 Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
 165 170 175
 Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
 180 185 190
 Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
 195 200 205
 Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
 210 215 220
 Ser Pro Gly Lys Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg
 225 230 235 240
 Gln Trp Leu Ala Ala Arg Ala Gly Gly Gly Gly Gly Gly Gly Ile
 245 250 255
 Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg
 260 265

<210> 9

<211> 855

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TMP-TMP-Fc

<220>

<221> CDS

<222> (39) .. (845)

<400> 9

tctagatttg ttttaactaa ttaaaggagg aataacat atg atc gaa ggt ccg act 56
 Met Ile Glu Gly Pro Thr

| | | | | | | | | | | | | | | | 1 | | | | | | | | | | | | | | | | 5 | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|--|
| ctg | cgt | cag | tgg | ctg | gct | gct | cgt | gct | ggc | ggt | ggt | ggc | gga | ggg | ggt | 104 | | | | | | | | | | | | | | | | |
| Leu | Arg | Gln | Trp | Leu | Ala | Ala | Arg | Ala | Gly | Gly | Gly | Gly | Gly | Gly | Gly | | | | | | | | | | | | | | | | | |
| | | | | 10 | | | | | 15 | | | | | 20 | | | | | | | | | | | | | | | | | | |
| ggc | att | gag | ggc | cca | acc | ctt | cgc | caa | tgg | ctt | gca | gca | cgc | gca | ggg | 152 | | | | | | | | | | | | | | | | |
| Gly | Ile | Glu | Gly | Pro | Thr | Leu | Arg | Gln | Trp | Leu | Ala | Ala | Arg | Ala | Gly | | | | | | | | | | | | | | | | | |
| | | | | 25 | | | | | 30 | | | | | 35 | | | | | | | | | | | | | | | | | | |
| gga | ggc | ggt | ggg | gac | aaa | act | cac | aca | tgt | cca | cct | tgc | cca | gca | cct | 200 | | | | | | | | | | | | | | | | |
| Gly | Gly | Gly | Gly | Asp | Lys | Thr | His | Thr | Cys | Pro | Pro | Cys | Pro | Ala | Pro | | | | | | | | | | | | | | | | | |
| | | | | 40 | | | | | 45 | | | | | 50 | | | | | | | | | | | | | | | | | | |
| gaa | ctc | ctg | ggg | gga | ccg | tca | gtt | ttc | ctc | ttc | ccc | cca | aaa | ccc | aag | 248 | | | | | | | | | | | | | | | | |
| Glu | Leu | Leu | Gly | Gly | Pro | Ser | Val | Phe | Leu | Phe | Pro | Pro | Lys | Pro | Lys | | | | | | | | | | | | | | | | | |
| 55 | | | | | 60 | | | | | 65 | | | | | 70 | | | | | | | | | | | | | | | | | |
| gac | acc | ctc | atg | atc | tcc | cgg | acc | cct | gag | gtc | aca | tgc | gtg | gtg | gtg | 296 | | | | | | | | | | | | | | | | |
| Asp | Thr | Leu | Met | Ile | Ser | Arg | Thr | Pro | Glu | Val | Thr | Cys | Val | Val | Val | | | | | | | | | | | | | | | | | |
| | | | | 75 | | | | | 80 | | | | | 85 | | | | | | | | | | | | | | | | | | |
| gac | gtg | agc | cac | gaa | gac | cct | gag | gtc | aag | ttc | aac | tgg | tac | gtg | gac | 344 | | | | | | | | | | | | | | | | |
| Asp | Val | Ser | His | Glu | Asp | Pro | Glu | Val | Lys | Phe | Asn | Trp | Tyr | Val | Asp | | | | | | | | | | | | | | | | | |
| | | | | 90 | | | | | 95 | | | | | 100 | | | | | | | | | | | | | | | | | | |
| ggc | gtg | gag | gtg | cat | aat | gcc | aag | aca | aag | ccg | cgg | gag | gag | cag | tac | 392 | | | | | | | | | | | | | | | | |
| Gly | Val | Glu | Val | His | Asn | Ala | Lys | Thr | Lys | Pro | Arg | Glu | Glu | Gln | Tyr | | | | | | | | | | | | | | | | | |
| | | | | 105 | | | | | 110 | | | | | 115 | | | | | | | | | | | | | | | | | | |
| aac | agc | acg | tac | cgt | gtg | gtc | agc | gtc | ctc | acc | gtc | ctg | cac | cag | gac | 440 | | | | | | | | | | | | | | | | |
| Asn | Ser | Thr | Tyr | Arg | Val | Val | Ser | Val | Leu | Thr | Val | Leu | His | Gln | Asp | | | | | | | | | | | | | | | | | |
| | | | | 120 | | | | | 125 | | | | | 130 | | | | | | | | | | | | | | | | | | |
| tgg | ctg | aat | ggc | aag | gag | tac | aag | tgc | aag | gtc | tcc | aac | aaa | gcc | ctc | 488 | | | | | | | | | | | | | | | | |
| Trp | Leu | Asn | Gly | Lys | Glu | Tyr | Lys | Cys | Lys | Val | Ser | Asn | Lys | Ala | Leu | | | | | | | | | | | | | | | | | |
| 135 | | | | | 140 | | | | | 145 | | | | | 150 | | | | | | | | | | | | | | | | | |
| cca | gcc | ccc | atc | gag | aaa | acc | atc | tcc | aaa | gcc | aaa | ggg | cag | ccc | cga | 536 | | | | | | | | | | | | | | | | |
| Pro | Ala | Pro | Ile | Glu | Lys | Thr | Ile | Ser | Lys | Ala | Lys | Gly | Gln | Pro | Arg | | | | | | | | | | | | | | | | | |
| | | | | 155 | | | | | 160 | | | | | 165 | | | | | | | | | | | | | | | | | | |
| gaa | cca | cag | gtg | tac | acc | ctg | ccc | cca | tcc | cgg | gat | gag | ctg | acc | aag | 584 | | | | | | | | | | | | | | | | |
| Glu | Pro | Gln | Val | Tyr | Thr | Leu | Pro | Pro | Ser | Arg | Asp | Glu | Leu | Thr | Lys | | | | | | | | | | | | | | | | | |
| | | | | 170 | | | | | 175 | | | | | 180 | | | | | | | | | | | | | | | | | | |
| aac | cag | gtc | agc | ctg | acc | tgc | ctg | gtc | aaa | ggc | ttc | tat | ccc | agc | gac | 632 | | | | | | | | | | | | | | | | |
| Asn | Gln | Val | Ser | Leu | Thr | Cys | Leu | Val | Lys | Gly | Phe | Tyr | Pro | Ser | Asp | | | | | | | | | | | | | | | | | |

| 185 | 190 | 195 | |
|---|-----|-----|-----|
| atc gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag | | | 680 |
| Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys | | | |
| 200 | 205 | 210 | |
| acc acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc | | | 728 |
| Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser | | | |
| 215 | 220 | 225 | 230 |
| aag ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca | | | 776 |
| Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser | | | |
| 235 | 240 | 245 | |
| tgc tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc | | | 824 |
| Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser | | | |
| 250 | 255 | 260 | |
| ctc tcc ctg tct ccg ggt aaa taatggatcc | | | 855 |
| Leu Ser Leu Ser Pro Gly Lys | | | |
| 265 | | | |

<210> 10

<211> 269

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:TMP-TMP-Fc

<400> 10

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ile | Glu | Gly | Pro | Thr | Leu | Arg | Gln | Trp | Leu | Ala | Ala | Arg | Ala | Gly |
| 1 | | | | 5 | | | | 10 | | | | | 15 | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Gly | Gly | Gly | Gly | Gly | Gly | Ile | Glu | Gly | Pro | Thr | Leu | Arg | Gln | Trp |
| | | 20 | | | | | 25 | | | | | | 30 | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Ala | Ala | Arg | Ala | Gly | Gly | Gly | Gly | Gly | Asp | Lys | Thr | His | Thr | Cys |
| | | 35 | | | | | 40 | | | | | 45 | | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Pro | Pro | Cys | Pro | Ala | Pro | Glu | Leu | Leu | Gly | Gly | Pro | Ser | Val | Phe | Leu |
| | | 50 | | | | 55 | | | | | 60 | | | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Pro | Pro | Lys | Pro | Lys | Asp | Thr | Leu | Met | Ile | Ser | Arg | Thr | Pro | Glu |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Thr | Cys | Val | Val | Val | Asp | Val | Ser | His | Glu | Asp | Pro | Glu | Val | Lys |
| | | | | 85 | | | | | 90 | | | | | 95 | |

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
 100 105 110
 Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
 115 120 125
 Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
 130 135 140
 Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
 145 150 155 160
 Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
 165 170 175
 Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
 180 185 190
 Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
 195 200 205
 Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
 210 215 220
 Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
 225 230 235 240
 Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
 245 250 255
 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 260 265

<210> 11

<211> 789

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TMP-Fc

<220>

<221> CDS

<222> (39) ... (779)

<400> 11


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tctagatttg ttttaactaa tttaaaggagg aataacat atg atc gaa ggt ccg act 56
                                   Met Ile Glu Gly Pro Thr
                                   1           5

ctg cgt cag tgg ctg gct gct cgt gct ggt gga ggc ggt ggg gac aaa 104
Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly Gly Gly Gly Asp Lys
      10           15           20

act cac aca tgt cca cct tgc cca gca cct gaa ctc ctg ggg gga ccg 152
Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
      25           30           35

tca gtt ttc ctc ttc ccc cca aaa ccc aag gac acc ctc atg atc tcc 200
Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
      40           45           50

cgg acc cct gag gtc aca tgc gtg gtg gtg gac gtg agc cac gaa gac 248
Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
      55           60           65           70

cct gag gtc aag ttc aac tgg tac gtg gac ggc gtg gag gtg cat aat 296
Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
      75           80           85

gcc aag aca aag ccg cgg gag gag cag tac aac agc acg tac cgt gtg 344
Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
      90           95           100

gtc agc gtc ctc acc gtc ctg cac cag gac tgg ctg aat ggc aag gag 392
Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
      105           110           115

tac aag tgc aag gtc tcc aac aaa gcc ctc cca gcc ccc atc gag aaa 440
Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
      120           125           130

acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca cag gtg tac acc 488
Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
      135           140           145           150

ctg ccc cca tcc cgg gat gag ctg acc aag aac cag gtc agc ctg acc 536
Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
      155           160           165

tgc ctg gtc aaa ggc ttc tat ccc agc gac atc gcc gtg gag tgg gag 584
Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
      170           175           180

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agc aat ggg cag ccg gag aac aac tac aag acc acg cct ccc gtg ctg 632
 Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 185 190 195

gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc acc gtg gac aag 680
 Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 200 205 210

agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc gtg atg cat gag 728
 Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 215 220 225 230

gct ctg cac aac cac tac acg cag aag agc ctc tcc ctg tct ccg ggt 776
 Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 235 240 245

aaa taatggatcc 789
 Lys

<210> 12

<211> 247

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:TMP-Fc

<400> 12

Met Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly
 1 5 10 15

Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
 20 25 30

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
 35 40 45

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
 50 55 60

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
 65 70 75 80

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
 85 90 95

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
 100 105 110

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
 115 120 125

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
 130 135 140

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
 145 150 155 160

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
 165 170 175

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
 180 185 190

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
 195 200 205

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
 210 215 220

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
 225 230 235 240

Leu Ser Leu Ser Pro Gly Lys
 245

<210> 13

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TMP

<400> 13

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
 1 5 10

<210> 14

<211> 36

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TMP-TMP

<400> 14

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
 1 5 10 15

Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu
 20 25 30

Ala Ala Arg Ala
 35

<210> 15

<211> 812

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-EMP

<220>

<221> CDS

<222> (39)..(797)

<400> 15

tctagatttg ttttaactaa ttaaaggagg aataacat atg gac aaa act cac aca 56
 Met Asp Lys Thr His Thr
 1 5

tgt cca cct tgt cca gct ccg gaa ctc ctg ggg gga ccg tca gtc ttc 104
 Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
 10 15 20

ctc ttc ccc cca aaa ccc aag gac acc ctc atg atc tcc cgg acc cct 152
 Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
 25 30 35

gag gtc aca tgc gtg gtg gtg gac gtg agc cac gaa gac cct gag gtc 200
 Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
 40 45 50

aag ttc aac tgg tac gtg gac ggc gtg gag gtg cat aat gcc aag aca 248
 Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
 55 60 65 70

aag ccg cgg gag gag cag tac aac agc acg tac cgt gtg gtc agc gtc 296
Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
75 80 85

ctc acc gtc ctg cac cag gac tgg ctg aat ggc aag gag tac aag tgc 344
Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
90 95 100

aag gtc tcc aac aaa gcc ctc cca gcc ccc atc gag aaa acc atc tcc 392
Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
105 110 115

aaa gcc aaa ggg cag ccc cga gaa cca cag gtg tac acc ctg ccc cca 440
Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
120 125 130

tcc cgg gat gag ctg acc aag aac cag gtc agc ctg acc tgc ctg gtc 488
Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
135 140 145 150

aaa ggc ttc tat ccc agc gac atc gcc gtg gag tgg gag agc aat ggg 536
Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
155 160 165

cag ccg gag aac aac tac aag acc acg cct ccc gtg ctg gac tcc gac 584
Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
170 175 180

ggc tcc ttc ttc ctc tac agc aag ctc acc gtg gac aag agc agg tgg 632
Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
185 190 195

cag cag ggg aac gtc ttc tca tgc tcc gtg atg cat gag gct ctg cac 680
Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
200 205 210

aac cac tac acg cag aag agc ctc tcc ctg tct ccg ggt aaa ggt gga 728
Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly
215 220 225 230

ggt ggt ggt gga ggt act tac tct tgc cac ttc ggc ccg ctg act tgg 776
Gly Gly Gly Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp
235 240 245

gtt tgc aaa ccg cag ggt ggt taatctcgtg gatcc 812
Val Cys Lys Pro Gln Gly Gly
250

<210> 16

<211> 253

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc-EMP

<400> 16

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
 1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
 20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
 65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
 85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
 100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
 115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
 130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
 145 150 155 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
 165 170 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
 180 185 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
 195 200 205

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 210 | | | | | 215 | | | | | 220 | | | | | | |
| Ser | Pro | Gly | Lys | Gly | Gly | Gly | Gly | Gly | Gly | Gly | Thr | Tyr | Ser | Cys | His | |
| 225 | | | | | 230 | | | | | 235 | | | | | | 240 |
| | | | | | | | | | | | | | | | | |
| Phe | Gly | Pro | Leu | Thr | Trp | Val | Cys | Lys | Pro | Gln | Gly | Gly | | | | |
| | | | | 245 | | | | | 250 | | | | | | | |

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<210> 17
<211> 807
<212> DNA
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence:EMP-Fc

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<220>  
<221> CDS  
<222> (39) .. (797)
```

<400> 17
tctagatttg ttttaactaa ttaaaggagg aataacat atg gga ggt act tac tct .56
Met Gly Gly Thr Tyr Ser
1 5

tgc cac ttc ggc ccg ctg act tgg gta tgt aag cca caa ggg ggt ggg 104
Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Gly
10 15 20

gga ggc ggg ggg gac aaa act cac aca tgt cca cct tgc cca gca cct 152
Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
25 30 35

gaa ctc ctg ggg gga ccg tca gtt ttc ctc ttc ccc cca aaa ccc aag 200
Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
40 45 50

gac acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg 248
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
55 60 65 70

gac gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac 296
Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
75 80 85

ggc gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac 344

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
 90 95 100

aac agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac 392
 Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
 105 110 115

tgg ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc 440
 Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
 120 125 130

cca gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga 488
 Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
 135 140 145 150

gaa cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag 536
 Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
 155 160 165

aac cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac 584
 Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
 170 175 180

atc gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag 632
 Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
 185 190 195

acc acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc 680
 Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
 200 205 210

aag ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca 728
 Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
 215 220 225 230

tgc tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc 776
 Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
 235 240 245

ctc tcc ctg tct ccg ggt aaa taatggatcc 807
 Leu Ser Leu Ser Pro Gly Lys
 250

<210> 18

<211> 253

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:EMP-Fc

<400> 18

| | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Gly | Gly | Thr | Tyr | Ser | Cys | His | Phe | Gly | Pro | Leu | Thr | Trp | Val | Cys | 1 | 5 | 10 | 15 |
| Lys | Pro | Gln | Gly | Gly | Gly | Gly | Gly | Gly | Gly | Asp | Lys | Thr | His | Thr | Cys | 20 | 25 | 30 | |
| Pro | Pro | Cys | Pro | Ala | Pro | Glu | Leu | Leu | Gly | Gly | Pro | Ser | Val | Phe | Leu | 35 | 40 | 45 | |
| Phe | Pro | Pro | Lys | Pro | Lys | Asp | Thr | Leu | Met | Ile | Ser | Arg | Thr | Pro | Glu | 50 | 55 | 60 | |
| Val | Thr | Cys | Val | Val | Val | Asp | Val | Ser | His | Glu | Asp | Pro | Glu | Val | Lys | 65 | 70 | 75 | 80 |
| Phe | Asn | Trp | Tyr | Val | Asp | Gly | Val | Glu | Val | His | Asn | Ala | Lys | Thr | Lys | 85 | 90 | 95 | |
| Pro | Arg | Glu | Glu | Gln | Tyr | Asn | Ser | Thr | Tyr | Arg | Val | Val | Ser | Val | Leu | 100 | 105 | 110 | |
| Thr | Val | Leu | His | Gln | Asp | Trp | Leu | Asn | Gly | Lys | Glu | Tyr | Lys | Cys | Lys | 115 | 120 | 125 | |
| Val | Ser | Asn | Lys | Ala | Leu | Pro | Ala | Pro | Ile | Glu | Lys | Thr | Ile | Ser | Lys | 130 | 135 | 140 | |
| Ala | Lys | Gly | Gln | Pro | Arg | Glu | Pro | Gln | Val | Tyr | Thr | Leu | Pro | Pro | Ser | 145 | 150 | 155 | 160 |
| Arg | Asp | Glu | Leu | Thr | Lys | Asn | Gln | Val | Ser | Leu | Thr | Cys | Leu | Val | Lys | 165 | 170 | 175 | |
| Gly | Phe | Tyr | Pro | Ser | Asp | Ile | Ala | Val | Glu | Trp | Glu | Ser | Asn | Gly | Gln | 180 | 185 | 190 | |
| Pro | Glu | Asn | Asn | Tyr | Lys | Thr | Thr | Pro | Pro | Val | Leu | Asp | Ser | Asp | Gly | 195 | 200 | 205 | |
| Ser | Phe | Phe | Leu | Tyr | Ser | Lys | Leu | Thr | Val | Asp | Lys | Ser | Arg | Trp | Gln | 210 | 215 | 220 | |
| Gln | Gly | Asn | Val | Phe | Ser | Cys | Ser | Val | Met | His | Glu | Ala | Leu | His | Asn | 225 | 230 | 235 | 240 |

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 245 250

<210> 19
 <211> 881
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:EMP-EMP-Fc

<220>
 <221> CDS
 <222> (41)..(871)

<400> 19
 tctagatttg agttttaact tttagaagga ggaataaaat atg gga ggt act tac 55
 Met Gly Gly Thr Tyr
 1 5

tct tgc cac ttc ggc cca ctg act tgg gtt tgc aaa ccg cag ggt ggc 103
 Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly
 10 15 20

ggc ggc ggc ggc ggt ggt acc tat tcc tgt cat ttt ggc ccg ctg acc 151
 Gly Gly Gly Gly Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr
 25 30 35

tgg gta tgt aag cca caa ggg ggt ggg gga ggc ggg ggg gac aaa act 199
 Trp Val Cys Lys Pro Gln Gly Gly Gly Gly Gly Gly Gly Asp Lys Thr
 40 45 50

cac aca tgt cca cct tgc cca gca cct gaa ctc ctg ggg gga ccg tca 247
 His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
 55 60 65

gtt ttc ctc ttc ccc cca aaa ccc aag gac acc ctc atg atc tcc cgg 295
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 70 75 80 85

acc cct gag gtc aca tgc gtg gtg gtg gac gtg agc cac gaa gac cct 343
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
 90 95 100

gag gtc aag ttc aac tgg tac gtg gac ggc gtg gag gtg cat aat gcc 391
 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala

| 105 | 110 | 115 | |
|---|-----|-----|-----|
| aag aca aag ccg cgg gag gag cag tac aac agc acg tac cgt gtg gtc | | | 439 |
| Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val | | | |
| 120 | 125 | 130 | |
| agc gtc ctc acc gtc ctg cac cag gac tgg ctg aat ggc aag gag tac | | | 487 |
| Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr | | | |
| 135 | 140 | 145 | |
| aag tgc aag gtc tcc aac aaa gcc ctc cca gcc ccc atc gag aaa acc | | | 535 |
| Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr | | | |
| 150 | 155 | 160 | 165 |
| atc tcc aaa gcc aaa ggg cag ccc cga gaa cca cag gtg tac acc ctg | | | 583 |
| Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu | | | |
| 170 | 175 | 180 | |
| ccc cca tcc cgg gat gag ctg acc aag aac cag gtc agc ctg acc tgc | | | 631 |
| Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys | | | |
| 185 | 190 | 195 | |
| ctg gtc aaa ggc ttc tat ccc agc gac atc gcc gtg gag tgg gag agc | | | 679 |
| Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser | | | |
| 200 | 205 | 210 | |
| aat ggg cag ccg gag aac aac tac aag acc acg cct ccc gtg ctg gac | | | 727 |
| Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp | | | |
| 215 | 220 | 225 | |
| tcc gac ggc tcc ttc ttc ctc tac agc aag ctc acc gtg gac aag agc | | | 775 |
| Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser | | | |
| 230 | 235 | 240 | 245 |
| agg tgg cag cag ggg aac gtc ttc tca tgc tcc gtg atg cat gag gct | | | 823 |
| Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala | | | |
| 250 | 255 | 260 | |
| ctg cac aac cac tac acg cag aag agc ctc tcc ctg tct ccg ggt aaa | | | 871 |
| Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys | | | |
| 265 | 270 | 275 | |
| taatggatcc | | | 881 |

<210> 20
 <211> 277
 <212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:EMP-EMP-Fc

<400> 20

Met Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys
 1 5 10 15

Lys Pro Gln Gly Gly Gly Gly Gly Gly Gly Gly Thr Tyr Ser Cys His
 20 25 30

Phe Gly Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Gly Gly Gly
 35 40 45

Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
 50 55 60

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 65 70 75 80

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 85 90 95

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 100 105 110

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
 115 120 125

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
 130 135 140

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
 145 150 155 160

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
 165 170 175

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
 180 185 190

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 195 200 205

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 210 215 220

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 225 230 235 240

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
 245 250 255

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 260 265 270

Leu Ser Pro Gly Lys
 275

<210> 21

<211> 884

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-EMP-EMP

<220>

<221> CDS

<222> (39)..(869)

<400> 21

tctagatttg ttttaactaa ttaaaggagg aataacat atg gac aaa act cac aca 56
 Met Asp Lys Thr His Thr
 1 5

tgt cca cct tgc cca gca cct gaa ctc ctg ggg gga ccg tca gtt ttc 104
 Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
 10 15 20

ctc ttc ccc cca aaa ccc aag gac acc ctc atg atc tcc cgg acc cct 152
 Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
 25 30 35

gag gtc aca tgc gtg gtg gtg gac gtg agc cac gaa gac cct gag gtc 200
 Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
 40 45 50

aag ttc aac tgg tac gtg gac ggc gtg gag gtg cat aat gcc aag aca 248
 Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
 55 60 65 70

aag ccg cgg gag gag cag tac aac agc acg tac cgt gtg gtc agc gtc 296
 Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
 75 80 85

| | |
|---|-----|
| ctc acc gtc ctg cac cag gac tgg ctg aat ggc aag gag tac aag tgc | 344 |
| Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys | |
| 90 95 100 | |
| aag gtc tcc aac aaa gcc ctc cca gcc ccc atc gag aaa acc atc tcc | 392 |
| Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser | |
| 105 110 115 | |
| aaa gcc aaa ggg cag ccc cga gaa cca cag gtg tac acc ctg cct cca | 440 |
| Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro | |
| 120 125 130 | |
| tcc cgg gat gag ctg acc aag aac cag gtc agc ctg acc tgc ctg gtc | 488 |
| Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val | |
| 135 140 145 150 | |
| aaa ggc ttc tat ccc agc gac atc gcc gtg gag tgg gag agc aat ggg | 536 |
| Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly | |
| 155 160 165 | |
| cag ccg gag aac aac tac aag acc acg cct ccc gtg ctg gac tcc gac | 584 |
| Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp | |
| 170 175 180 | |
| ggc tcc ttc ttc ctc tac agc aag ctc acc gtg gac aag agc agg tgg | 632 |
| Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp | |
| 185 190 195 | |
| cag cag ggg aac gtc ttc tca tgc tcc gtg atg cat gag gct ctg cac | 680 |
| Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His | |
| 200 205 210 | |
| aac cac tac acg cag aag agc ctc tcc ctg tct ccg ggt aaa ggt gga | 728 |
| Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly | |
| 215 220 225 230 | |
| ggt ggt ggc gga ggt act tac tct tgc cac ttc ggc cca ctg act tgg | 776 |
| Gly Gly Gly Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp | |
| 235 240 245 | |
| gtt tgc aaa ccg cag ggt ggc ggc ggc ggc ggc ggt ggt acc tat tcc | 824 |
| Val Cys Lys Pro Gln Gly Gly Gly Gly Gly Gly Gly Gly Thr Tyr Ser | |
| 250 255 260 | |
| tgt cat ttt ggc ccg ctg acc tgg gta tgt aag cca caa ggg ggt | 869 |
| Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly | |
| 265 270 275 | |

taatctcgag gatcc

884

<210> 22

<211> 277

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc-EMP-EMP

<400> 22

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145 150 155 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
165 170 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
180 185 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val

195 200 205
 Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
 210 215 220
 Ser Pro Gly Lys Gly Gly Gly Gly Gly Gly Thr Tyr Ser Cys His
 225 230 235 240
 Phe Gly Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Gly Gly Gly
 245 250 255
 Gly Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys
 260 265 270
 Lys Pro Gln Gly Gly
 275

<210> 23

<211> 1545

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:pAMG216

<400> 23

cgtaacgtat gcatggtctc cccatgcgag agtagggaac tgccaggcat caaataaaac 60
 gaaaggctca gtcgaaagac tgggcctttc gttttatctg ttgtttgctg gtgaacgctc 120
 tcctgagtag gacaaatccg ccgggagcgg atttgaacgt tgcgaagcaa cggcccggag 180
 ggtggcgggc aggacgcccg ccataaactg ccaggcatca aattaagcag aaggccatcc 240
 tgacggatgg ccttttttgcg tttctacaaa ctcttttggt tatttttcta aatacattca 300
 aatatggacg tgcgtacttaa ctttttaaagt atgggcaatc aattgctcct gttaaaattg 360
 ctttagaaat actttggcag cggtttggtg tattgagttt catttgcgca ttggttaaat 420
 ggaaagtgc cgtgcgctta ctacagccta atatttttga aatatcccaa gagctttttc 480
 cttcgcatgc ccacgctaaa cattcttttt ctcttttggt taaatcgttg tttgatttat 540
 tatttgctat atttattttt cgataattat caactagaga aggaacaatt aatggtatgt 600
 tcatacacgc atgtaaaaat aaactatcta tatagttgtc tttctctgaa tgtgcaaaac 660
 taagcattcc gaagccatta ttagcagtat gaataggga actaaacca gtgataagac 720
 ctgatgattt cgcttcttta attacatttg gagatttttt atttacagca ttgttttcaa 780
 atatattcca attaatcggg gaatgattgg agttagaata atctactata ggatcatatt 840
 ttattaaatt agcgtcatca taatattgcc tccatttttt agggtaatta tccagaattg 900
 aaatatcaga tttaaccata gaatgaggat aaatgatcgc gagtaaataa tattcacaat 960
 gtaccatttt agtcatatca gataagcatt gattaatatc attattgctt ctacaggctt 1020
 taattttatt aattattctg taagtgtcgt cggcatttat gtctttcata ccca~~ct~~ctctt 1080
 tacccttacc tattgtttgt cgcaagtttt gcgtgttata tatcattaaa acggtaatatg 1140
 attgacattt gattctaata aattggattt ttgtcacact attatatcgc ttgaaataca 1200


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attgtttaac ataagtacct gtaggatcgt acagggtttac gcaagaaaat ggtttggttat 1260
agtcgattaa tcgatttgat tctagatttg ttttaactaa ttaaaggagg aataacatat 1320
ggttaacgcg ttggaattcg agctcactag tgtcgacctg cagggtagca tggaagctta 1380
ctcgaggatc cgcggaaaga agaagaagaa gaagaaagcc cgaaaggaag ctgagttggc 1440
tgctgccacc gctgagcaat aactagcata accccttggg gcctctaaac gggctcttgag 1500
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<210> 24

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 24

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Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Lys Ala
  1               5               10

```

<210> 25

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 25

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Ile Glu Gly Pro Thr Leu Arg Glu Trp Leu Ala Ala Arg Ala
  1               5               10

```

<210> 26

<211> 29

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<220>

<223> At position 15, Xaa=a linker sequence of 1 to 20 amino acids

<400> 26

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Xaa Ile
1 5 10 15

Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
20 25

<210> 27

<211> 29

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC PEPTIDE

<220>

<223> At position 15, Xaa=a linker sequence of 1 to 20 amino acids

<400> 27

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Lys Ala Xaa Ile
1 5 10 15

Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Lys Ala
20 25

<210> 28

<211> 29

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC PEPTIDE

<220>

<223> At position 9 disulfide linkage with residue 24

<220>

<223> At position 24 disulfide linkage with residue 9

<400> 28

Ile Glu Gly Pro Thr Leu Arg Gln Cys Leu Ala Ala Arg Ala Xaa Ile
1 5 10 15

Glu Gly Pro Thr Leu Arg Gln Cys Leu Ala Ala Arg Ala
20 25

<210> 29

<211> 31

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<220>

<223> At position 16 bromoacetyl group linked to
sidechain

<400> 29

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Xaa Lys
1 5 10 15

Xaa Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
20 25 30

<210> 30

<211> 31

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<220>

<223> At position 16 polyethylene glycol linked to
sidechain

<400> 30

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Xaa Lys
1 5 10 15

Xaa Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
20 25 30

<210> 31

<211> 29

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<220>

<223> At position 9 disulfide bond to residue 9 of a
separate identical sequence

<400> 31

Ile Glu Gly Pro Thr Leu Arg Gln Cys Leu Ala Ala Arg Ala Xaa Ile
1 5 10 15

Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
20 25

<210> 32

<211> 29

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<220>

<223> At position 24 disulfide bond to residue 9 of a
separate identical sequence

<400> 32

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Xaa Ile
1 5 10 15

Glu Gly Pro Thr Leu Arg Gln Cys Leu Ala Ala Arg Ala
20 25

<210> 33
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 33
Val Arg Asp Gln Ile Xaa Xaa Xaa Leu
1 5

<210> 34
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 34
Thr Leu Arg Glu Trp Leu
1 5

<210> 35
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 35
Gly Arg Val Arg Asp Gln Val Ala Gly Trp
1 5 10

<210> 36

<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 36

Gly Arg Val Lys Asp Gln Ile Ala Gln Leu
1 5 10

<210> 37
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Description of
Artificial SequenceTPO-MIMETIC PEPTIDE

<400> 37

Gly Val Arg Asp Gln Val Ser Trp Ala Leu
1 5 10

<210> 38
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 38

Glu Ser Val Arg Glu Gln Val Met Lys Tyr
1 5 10

<210> 39
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 39

Ser Val Arg Ser Gln Ile Ser Ala Ser Leu
1 5 10

<210> 40

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 40

Gly Val Arg Glu Thr Val Tyr Arg His Met
1 5 10

<210> 41

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 41

Gly Val Arg Glu Val Ile Val Met His Met Leu
1 5 10

<210> 42

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC

PEPTIDE

<400> 42

Gly Arg Val Arg Asp Gln Ile Trp Ala Ala Leu
1 5 10

<210> 43

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 43

Ala Gly Val Arg Asp Gln Ile Leu Ile Trp Leu
1 5 10

<210> 44

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 44

Gly Arg Val Arg Asp Gln Ile Met Leu Ser Leu
1 5 10

<210> 45

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 45

Gly Arg Val Arg Asp Gln Ile Xaa Xaa Xaa Leu
1 5 10

<210> 46

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 46

Cys Thr Leu Arg Gln Trp Leu Gln Gly Cys
1 5 10

<210> 47

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 47

Cys Thr Leu Gln Glu Phe Leu Glu Gly Cys
1 5 10

<210> 48

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 48

Cys Thr Arg Thr Glu Trp Leu His Gly Cys
1 5 10

<210> 49
<211> 12
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 49

Cys Thr Leu Arg Glu Trp Leu His Gly Gly Phe Cys
1 5 10

<210> 50
<211> 12
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TMP

<400> 50

Cys Thr Leu Arg Glu Trp Val Phe Ala Gly Leu Cys
1 5 10

<210> 51
<211> 13
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TMP

<400> 51

Cys Thr Leu Arg Gln Trp Leu Ile Leu Leu Gly Met Cys
1 5 10

<210> 52
<211> 14
<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 52

Cys Thr Leu Ala Glu Phe Leu Ala Ser Gly Val Glu Gln Cys
1 5 10

<210> 53

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TMP

<400> 53

Cys Ser Leu Gln Glu Phe Leu Ser His Gly Gly Tyr Val Cys
1 5 10

<210> 54

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TMP

<400> 54

Cys Thr Leu Arg Glu Phe Leu Asp Pro Thr Thr Ala Val Cys
1 5 10

<210> 55

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 55

Cys Thr Leu Lys Glu Trp Leu Val Ser His Glu Val Trp Cys
1 5 10

<210> 56

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 56

Cys Thr Leu Arg Glu Trp Leu Xaa Xaa Cys
1 5 10

<210> 57

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 57

Cys Thr Leu Arg Glu Trp Leu Xaa Xaa Xaa Cys
1 5 10

<210> 58

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 58

Cys Thr Leu Arg Glu Trp Leu Xaa Xaa Xaa Xaa Cys

1

5

10

<210> 59

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 59

Cys Thr Leu Arg Glu Trp Leu Xaa Xaa Xaa Xaa Cys
1 5 10

<210> 60

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 60

Cys Thr Leu Arg Glu Trp Leu Xaa Xaa Xaa Xaa Xaa Cys
1 5 10

<210> 61

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 61

Arg Glu Gly Pro Thr Leu Arg Gln Trp Met
1 5 10

<210> 62
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 62

Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala
1 5 10

<210> 63
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 63

Glu Arg Gly Pro Phe Trp Ala Lys Ala Cys
1 5 10

<210> 64
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 64

Arg Glu Gly Pro Arg Cys Val Met Trp Met
1 5 10

<210> 65
<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 65

Cys Gly Thr Glu Gly Pro Thr Leu Ser Thr Trp Leu Asp Cys
1 5 10

<210> 66

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 66

Cys Glu Gln Asp Gly Pro Thr Leu Leu Glu Trp Leu Lys Cys
1 5 10

<210> 67

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 67

Cys Glu Leu Val Gly Pro Ser Leu Met Ser Trp Leu Thr Cys
1 5 10

<210> 68

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 68

Cys Leu Thr Gly Pro Phe Val Thr Gln Trp Leu Tyr Glu Cys
1 5 10

<210> 69

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 69

Cys Arg Ala Gly Pro Thr Leu Leu Glu Trp Leu Thr Leu Cys
1 5 10

<210> 70

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 70

Cys Ala Asp Gly Pro Thr Leu Arg Glu Trp Ile Ser Phe Cys
1 5 10

<210> 71

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 71

Cys Xaa Glu Gly Pro Thr Leu Arg Glu Trp Leu Xaa Cys
1 5 10

<210> 72

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 72

Cys Xaa Xaa Glu Gly Pro Thr Leu Arg Glu Trp Leu Xaa Cys
1 5 10

<210> 73

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 73

Cys Xaa Glu Gly Pro Thr Leu Arg Glu Trp Leu Xaa Xaa Cys
1 5 10

<210> 74

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 74

Cys Xaa Xaa Glu Gly Pro Thr Leu Arg Glu Trp Leu Xaa Xaa Cys

1

5

10

15

<210> 75

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 75

Gly Gly Cys Thr Leu Arg Glu Trp Leu His Gly Gly Phe Cys Gly Gly
1 5 10 15

<210> 76

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 76

Gly Gly Cys Ala Asp Gly Pro Thr Leu Arg Glu Trp Ile Ser Phe Cys
1 5 10 15

Gly Gly

<210> 77

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 77

Gly Asn Ala Asp Gly Pro Thr Leu Arg Gln Trp Leu Glu Gly Arg Arg

1

5

10

15

Pro Lys Asn

<210> 78

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 78

Leu Ala Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu His Gly Asn Gly
1 5 10 15

Arg Asp Thr

<210> 79

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 79

His Gly Arg Val Gly Pro Thr Leu Arg Glu Trp Lys Thr Gln Val Ala
1 5 10 15

Thr Lys Lys

<210> 80

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 80

Thr Ile Lys Gly Pro Thr Leu Arg Gln Trp Leu Lys Ser Arg Glu His
1 5 10 15

Thr Ser

<210> 81

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 81

Ile Ser Asp Gly Pro Thr Leu Lys Glu Trp Leu Ser Val Thr Arg Gly
1 5 10 15

Ala Ser

<210> 82

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 82

Ser Ile Glu Gly Pro Thr Leu Arg Glu Trp Leu Thr Ser Arg Thr Pro
1 5 10 15

His Ser

<210> 83
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 83
Tyr Xaa Cys Xaa Xaa Gly Pro Xaa Thr Trp Xaa Cys Xaa Pro
1 5 10

<210> 84
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 84
Tyr Xaa Cys Xaa Xaa Gly Pro Xaa Thr Trp Xaa Cys Xaa Pro Tyr Xaa
1 5 10 15

Cys Xaa Xaa Gly Pro Xaa Thr Trp Xaa Cys Xaa Pro
20 25

<210> 85
<211> 29
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<220>
<223> At position 15, Xaa=a linker sequence of 1 to 20
amino acids

<400> 85

Tyr Xaa Cys Xaa Xaa Gly Pro Xaa Thr Trp Xaa Cys Xaa Pro Xaa Tyr
1 5 10 15

Xaa Cys Xaa Xaa Gly Pro Xaa Thr Trp Xaa Cys Xaa Pro
20 25

<210> 86

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<220>

<223> At position 15 linked through epsilon amine to
lysyl, which is linked to a separate identical
sequence through that sequence's alpha amine

<400> 86

Tyr Xaa Cys Xaa Xaa Gly Pro Xaa Thr Trp Xaa Cys Xaa Pro
1 5 10

<210> 87

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 87

Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
1 5 10 15

Pro Gln Gly Gly
20

<210> 88

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 88

Gly Gly Asp Tyr His Cys Arg Met Gly Pro Leu Thr Trp Val Cys Lys
1 5 10 15Pro Leu Gly Gly
20

<210> 89

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 89

Gly Gly Val Tyr Ala Cys Arg Met Gly Pro Ile Thr Trp Val Cys Ser
1 5 10 15Pro Leu Gly Gly
20

<210> 90

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 90

Val Gly Asn Tyr Met Cys His Phe Gly Pro Ile Thr Trp Val Cys Arg
1 5 10 15

Pro Gly Gly Gly

20

<210> 91
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:EPO-MIMETIC
 PEPTIDE

<400> 91
 Gly Gly Leu Tyr Leu Cys Arg Phe Gly Pro Val Thr Trp Asp Cys Gly
 1 5 10 15
 Tyr Lys Gly Gly
 20

<210> 92
 <211> 40
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:EPO-MIMETIC
 PEPTIDE

<400> 92
 Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
 1 5 10 15
 Pro Gln Gly Gly Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr
 20 25 30
 Trp Val Cys Lys Pro Gln Gly Gly
 35 40

<210> 93
 <211> 41
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<220>

<223> At position 21, Xaa=a linker sequence of 1 to 20
amino acids

<400> 93

Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
1 5 10 15Pro Gln Gly Gly Xaa Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu
20 25 30Thr Trp Val Cys Lys Pro Gln Gly Gly
35 40

<210> 94

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 94

Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
1 5 10 15Pro Gln Gly Gly Ser Ser Lys
20

<210> 95

<211> 46

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<400> 95

Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
1 5 10 15

Pro Gln Gly Gly Ser Ser Lys Gly Gly Thr Tyr Ser Cys His Phe Gly
20 25 30

Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Ser Ser Lys
35 40 45

<210> 96

<211> 47

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDE

<220>

<223> At position 24, Xaa=a linker sequence of 1 to 20
amino acids

<400> 96

Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
1 5 10 15

Pro Gln Gly Gly Ser Ser Lys Xaa Gly Gly Thr Tyr Ser Cys His Phe
20 25 30

Gly Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Ser Ser Lys
35 40 45

<210> 97

<211> 22

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<220>

<223> At position 22 linked through epsilon amine to
lysyl, which is linked to a separate identical

sequence through that sequence's alpha amine

<400> 97

Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
1 5 10 15

Pro Gln Gly Gly Ser Ser
20

<210> 98

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<220>

<223> At position 23 biotin linked to the sidechain
through a linker

<400> 98

Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
1 5 10 15

Pro Gln Gly Gly Ser Ser Lys
20

<210> 99

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:G-CSF MIMETIC
PEPTIDE

<220>

<223> At position 4 disulfide bond to residue 4 of a
separate identical sequence

<400> 99

Glu Glu Asp Cys Lys

1

5

<210> 100

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:G-CSF MIMETIC
PEPTIDE

<220>

<223> At position 4, Xaa is an isoteric ethylene spacer
linked to a separate identical sequence

<400> 100

Glu Glu Asp Xaa Lys

1

5

<210> 101

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:G-CSF MIMETIC
PEPTIDE

<220>

<223> At position 1, Xaa is a pyroglutamic acid residue

<220>

<223> At position 4, Xaa is an isoteric ethylene spacer
linked to a separate identical sequence

<400> 101

Xaa Glu Asp Xaa Lys

1

5

<210> 102

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<220>

<223> At position 1, Xaa is a picolinic acid residue

<220>

<223> At position 4, Xaa is an isoteric ethylene spacer
linked to a separate identical sequence

<400> 102

Xaa Ser Asp Xaa Lys
1 5

<210> 103

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<220>

<223> At position 6, Xaa=a linker sequence of 1 to 20
amino acids

<400> 103

Glu Glu Asp Cys Lys Xaa Glu Glu Asp Cys Lys
1 5 10

<210> 104

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<220>

<223> At position 6, Xaa=a linker sequence of 1 to 20
amino acids

<400> 104

Glu Glu Asp Xaa Lys Xaa Glu Glu Asp Xaa Lys
1 5 10

<210> 105

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:ANTIVIRAL (HBV)
PEPTIDE

<400> 105

Leu Leu Gly Arg Met Lys
1 5

<210> 106

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST
PEPTIDE

<400> 106

Tyr Cys Phe Thr Ala Ser Glu Asn His Cys Tyr
1 5 10

<210> 107

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST
PEPTIDE

<400> 107

Tyr Cys Phe Thr Asn Ser Glu Asn His Cys Tyr
1 5 10

<210> 108

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST
PEPTIDE

<400> 108

Tyr Cys Phe Thr Arg Ser Glu Asn His Cys Tyr
1 5 10

<210> 109

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST
PEPTIDE

<400> 109

Phe Cys Ala Ser Glu Asn His Cys Tyr
1 5

<210> 110

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST
PEPTIDE

<400> 110

Tyr Cys Ala Ser Glu Asn His Cys Tyr
1 5

<210> 111
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST
PEPTIDE

<400> 111

Phe Cys Asn Ser Glu Asn His Cys Tyr
1 5

<210> 112
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST
PEPTIDE

<400> 112

Phe Cys Asn Ser Glu Asn Arg Cys Tyr
1 5

<210> 113
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST
PEPTIDE

<400> 113

Phe Cys Asn Ser Val Glu Asn Arg Cys Tyr
1 5 10

<210> 114
<211> 11
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST
PEPTIDE

<400> 114

Tyr Cys Ser Gln Ser Val Ser Asn Asp Cys Phe
1 5 10

<210> 115
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST
PEPTIDE

<400> 115

Phe Cys Val Ser Asn Asp Arg Cys Tyr
1 5

<210> 116
<211> 11
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST
PEPTIDE

<400> 116

Tyr Cys Arg Lys Glu Leu Gly Gln Val Cys Tyr
1 5 10

<210> 117
<211> 9
<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST

<400> 117

Tyr Cys Lys Glu Pro Gly Gln Cys Tyr

1

5

<210> 118

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST

<400> 118

Tyr Cys Arg Lys Glu Met Gly Cys Tyr

1

5

<210> 119

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST

<400> 119

Phe Cys Arg Lys Glu Met Gly Cys Tyr

1

5

<210> 120

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST

<400> 120

Tyr Cys Trp Ser Gln Asn Leu Cys Tyr
1 5

<210> 121
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:TNF-ANTAGONIST

<400> 121
Tyr Cys Glu Leu Ser Gln Tyr Leu Cys Tyr
1 5 10

<210> 122
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:TNF-ANTAGONIST

<400> 122
Tyr Cys Trp Ser Gln Asn Tyr Cys Tyr
1 5

<210> 123
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:TNF-ANTAGONIST

<400> 123
Tyr Cys Trp Ser Gln Tyr Leu Cys Tyr
1 5

<210> 124

<211> 37

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 124

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Gly Pro Xaa Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Thr Trp Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
20 25 30

Xaa Xaa Xaa Xaa Xaa
35

<210> 125

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CTLA4-MIMETIC
PEPTIDE

<400> 125

Gly Phe Val Cys Ser Gly Ile Phe Ala Val Gly Val Gly Arg Cys
1 5 10 15

<210> 126

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CTLA4-MIMETIC
PEPTIDE

<400> 126

Ala Pro Gly Val Arg Leu Gly Cys Ala Val Leu Gly Arg Tyr Cys
1 5 10 15

<210> 127

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:C3B ANTAGONIST

<400> 127

Ile Cys Val Val Gln Asp Trp Gly His His Arg Cys Thr Ala Gly His
1 5 10 15

Met Ala Asn Leu Thr Ser His Ala Ser Ala Ile
20 25

<210> 128

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:C3B ANTAGONIST
PEPTIDE

<400> 128

Ile Cys Val Val Gln Asp Trp Gly His His Arg Cys Thr
1 5 10

<210> 129

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:C3B ANTAGONIST
PEPTIDE

<400> 129

Cys Val Val Gln Asp Trp Gly His His Ala Cys
1 5 10

<210> 130
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 130
Thr Phe Ser Asp Leu Trp
1 5

<210> 131
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 131
Gln Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro
1 5 10

<210> 132
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 132
Gln Pro Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro
1 5 10

<210> 133
<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 133

Gln Glu Thr Phe Ser Asp Tyr Trp Lys Leu Leu Pro
1 5 10

<210> 134

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 134

Gln Pro Thr Phe Ser Asp Tyr Trp Lys Leu Leu Pro
1 5 10

<210> 135

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 135

Met Pro Arg Phe Met Asp Tyr Trp Glu Gly Leu Asn
1 5 10

<210> 136

<211> 12

<212> PRT...

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:C3B ANTAGONIST

<400> 136

| | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Gln | Asn | Phe | Ile | Asp | Tyr | Trp | Thr | Gln | Gln | Phe |
| 1 | | | | 5 | | | | | 10 | | |

<210> 137

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 137

| | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Thr | Gly | Pro | Ala | Phe | Thr | His | Tyr | Trp | Ala | Thr | Phe |
| 1 | | | | 5 | | | | | 10 | | |

<210> 138

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 138

| | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Asp | Arg | Ala | Pro | Thr | Phe | Arg | Asp | His | Trp | Phe | Ala | Leu | Val |
| 1 | | | | 5 | | | | | 10 | | | | 15 | |

<210> 139

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 139

Pro Arg Pro Ala Leu Val Phe Ala Asp Tyr Trp Glu Thr Leu Tyr
1 5 10 15

<210> 140

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 140

Pro Ala Phe Ser Arg Phe Trp Ser Asp Leu Ser Ala Gly Ala His
1 5 10 15

<210> 141

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 141

Pro Ala Phe Ser Arg Phe Trp Ser Lys Leu Ser Ala Gly Ala His
1 5 10 15

<210> 142

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 142

Pro Xaa Phe Xaa Asp Tyr Trp Xaa Xaa Leu
1 5 10

<210> 143
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 143
Gln Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro
1 5 10

<210> 144
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 144
Gln Pro Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro
1 5 10

<210> 145
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 145
Gln Glu Thr Phe Ser Asp Tyr Trp Lys Leu Leu Pro
1 5 10

<210> 146
<211> 12
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 146

Gln Pro Thr Phe Ser Asp Tyr Trp Lys Leu Leu Pro
1 5 10

<210> 147

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 147

Asp Ile Thr Trp Asp Gln Leu Trp Asp Leu Met Lys
1 5 10

<210> 148

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 148

Asp Ile Thr Trp Asp Glu Leu Trp Lys Ile Met Asn
1 5 10

<210> 149

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 149

Asp Tyr Thr Trp Phe Glu Leu Trp Asp Met Met Gln
1 5 10

<210> 150

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 150

Gln Ile Thr Trp Ala Gln Leu Trp Asn Met Met Lys
1 5 10

<210> 151

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 151

Asp Met Thr Trp His Asp Leu Trp Thr Leu Met Ser
1 5 10

<210> 152

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 152

Asp Tyr Ser Trp His Asp Leu Trp Glu Met Met Ser
1 5 10

<210> 153

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 153

Glu Ile Thr Trp Asp Gln Leu Trp Glu Val Met Asn
1 5 10

<210> 154

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MDM/HDM
ANTAGONIST PEPTIDE

<400> 154

His Val Ser Trp Glu Gln Leu Trp Asp Ile Met Asn
1 5 10

<210> 155

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 155

His Ile Thr Trp Asp Gln Leu Trp Arg Ile Met Thr
1 5 10

<210> 156

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 156

Arg Asn Met Ser Trp Leu Glu Leu Trp Glu His Met Lys
1 5 10

<210> 157

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN

<400> 157

Ala Glu Trp Thr Trp Asp Gln Leu Trp His Val Met Asn Pro Ala Glu
1 5 10 15

Ser Gln

<210> 158

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN

<400> 158

His Arg Ala Glu Trp Leu Ala Leu Trp Glu Gln Met Ser Pro

1 5 10

<210> 159
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 159
Lys Lys Glu Asp Trp Leu Ala Leu Trp Arg Ile Met Ser Val
1 5 10

<210> 160
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SELECTIN

<400> 160
Ile Thr Trp Asp Gln Leu Trp Asp Leu Met Lys
1 5 10

<210> 161
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SELECTIN

<400> 161
Asp Ile Thr Trp Asp Gln Leu Trp Asp Leu Met Lys
1 5 10

<210> 162

<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SELECTIN

<400> 162
Asp Ile Thr Trp Asp Gln Leu Trp Asp Leu Met Lys
1 5 10

<210> 163
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 163
Asp Ile Thr Trp Asp Gln Leu Trp Asp Leu Met Lys
1 5 10

<210> 164
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 164
Ser Cys Val Lys Trp Gly Lys Lys Glu Phe Cys Gly Ser
1 5 10

<210> 165
<211> 12
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN

<400> 165

Ser Cys Trp Lys Tyr Trp Gly Lys Glu Cys Gly Ser
1 5 10

<210> 166

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 166

Ser Cys Tyr Glu Trp Gly Lys Leu Arg Trp Cys Gly Ser
1 5 10

<210> 167

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: CALMODULIN
ANTAGONIST PEPTIDE

<400> 167

Ser Cys Leu Arg Trp Gly Lys Trp Ser Asn Cys Gly Ser
1 5 10

<210> 168

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 168

Ser Cys Trp Arg Trp Gly Lys Tyr Gln Ile Cys Gly Ser
1 5 10

<210> 169

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 169

Ser Cys Val Ser Trp Gly Ala Leu Lys Leu Cys Gly Ser
1 5 10

<210> 170

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 170

Ser Cys Ile Arg Trp Gly Gln Asn Thr Phe Cys Gly Ser
1 5 10

<210> 171

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 171

Ser Cys Trp Gln Trp Gly Asn Leu Lys Ile Cys Gly Ser
1 5 10

<210> 172
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 172
Ser Cys Val Arg Trp Gly Gln Leu Ser Ile Cys Gly Ser
1 5 10

<210> 173
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 173
Leu Lys Lys Phe Asn Ala Arg Arg Lys Leu Lys Gly Ala Ile Leu Thr
1 5 10 15

Thr Met Leu Ala Lys
20

<210> 174
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:CALMODULIN

<400> 174
Arg Arg Trp Lys Lys Asn Phe Ile Ala Val Ser Ala Ala Asn Arg Phe
1 5 10 15

Lys Lys

<210> 175

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN

<400> 175

Arg Lys Trp Gln Lys Thr Gly His Ala Val Arg Ala Ile Gly Arg Leu
1 5 10 15

Ser Ser

<210> 176

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 176

Ile Asn Leu Lys Ala Leu Ala Ala Leu Ala Lys Lys Ile Leu
1 5 10

<210> 177

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 177

Lys Ile Trp Ser Ile Leu Ala Pro Leu Gly Thr Thr Leu Val Lys Leu

| 1 | 5 | 10 | 15 |
|---------|---|----|----|
| Val Ala | | | |

```
<210> 178
<211> 14
<212> PRT
<213> Artificial Sequence
```

<220>
<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 178
Leu Lys Lys Leu Leu Lys Leu Leu Lys Lys Leu Leu Lys Leu
1 5 10

```
<210> 179
<211> 18
<212> PRT
<213> Artificial Sequence
```

<220>
<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 179
Leu Lys Trp Lys Lys Leu Leu Lys Leu Leu Lys Lys Leu Leu Lys Lys
1 5 10 15

Leu Leu

```
<210> 180
<211> 17
<212> PRT
<213> Artificial Sequence
```

<220> ...
<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 180

Ala Glu Trp Pro Ser Leu Thr Glu Ile Lys Thr Leu Ser His Phe Ser
1 5 10 15

Val

<210> 181

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 181

Ala Glu Trp Pro Ser Pro Thr Arg Val Ile Ser Thr Thr Tyr Phe Gly
1 5 10 15

Ser

<210> 182

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 182

Ala Glu Leu Ala His Trp Pro Pro Val Lys Thr Val Leu Arg Ser Phe
1 5 10 15

Thr

<210> 183

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 183

Ala Glu Gly Ser Trp Leu Gln Leu Leu Asn Leu Met Lys Gln Met Asn
1 5 10 15

Asn

<210> 184

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CALMODULIN
ANTAGONIST PEPTIDE

<400> 184

Ala Glu Trp Pro Ser Leu Thr Glu Ile Lys
1 5 10

<210> 185

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence:VINCULIN-BINDING PEPTIDE

<400> 185

Ser Thr Gly Gly Phe Asp Asp Val Tyr Asp Trp Ala Arg Gly Val Ser
1 5 10 15

Ser Ala Leu Thr Thr Thr Leu Val Ala Thr Arg
20 25

<210> 186
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial
Sequence:VINCULIN-BINDING PEPTIDE

<400> 186
Ser Thr Gly Gly Phe Asp Asp Val Tyr Asp Trp Ala Arg Arg Val Ser
1 5 10 15
Ser Ala Leu Thr Thr Thr Leu Val Ala Thr Arg
20 25

<210> 187
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VINCULIN
BINDING PEPTIDE

<400> 187
Ser Arg Gly Val Asn Phe Ser Glu Trp Leu Tyr Asp Met Ser Ala Ala
1 5 10 15
Met Lys Glu Ala Ser Asn Val Phe Pro Ser Arg Arg Ser Arg
20 25 30

<210> 188
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VINCULIN
BINDING PEPTIDE

<400> 188
Ser Ser Gln Asn Trp Asp Met Glu Ala Gly Val Glu Asp Leu Thr Ala

1 5 10 15
Ala Met Leu Gly Leu Leu Ser Thr Ile His Ser Ser Ser Arg
20 25 30

<210> 189
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VINCULIN
BINDING PEPTIDE

<400> 189
Ser Ser Pro Ser Leu Tyr Thr Gln Phe Leu Val Asn Tyr Glu Ser Ala
1 5 10 15

Ala Thr Arg Ile Gln Asp Leu Leu Ile Ala Ser Arg Pro Ser Arg
20 25 30

<210> 190
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VINCULIN
BINDING PEPTIDE

<400> 190
Ser Ser Thr Gly Trp Val Asp Leu Leu Gly Ala Leu Gln Arg Ala Ala
1 5 10 15

Asp Ala Thr Arg Thr Ser Ile Pro Pro Ser Leu Gln Asn Ser Arg
20 25 30

<210> 191
<211> 18
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VINCULIN
BINDING PEPTIDE

<400> 191

Asp Val Tyr Thr Lys Lys Glu Leu Ile Glu Cys Ala Arg Arg Val Ser
1 5 10 15

Glu Lys

<210> 192

<211> 22

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:C4BP-BINDING
PEPTIDE

<400> 192

Glu Lys Gly Ser Tyr Tyr Pro Gly Ser Gly Ile Ala Gln Phe His Ile
1 5 10 15Asp Tyr Asn Asn Val Ser
20

<210> 193

<211> 22

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:C4BP-BINDING
PEPTIDE

<400> 193

Ser Gly Ile Ala Gln Phe His Ile Asp Tyr Asn Asn Val Ser Ser Ala
1 5 10 15Glu Gly Trp His Val Asn
20

<210> 194
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:C4BP-BINDING
PEPTIDE

<400> 194
Leu Val Thr Val Glu Lys Gly Ser Tyr Tyr Pro Gly Ser Gly Ile Ala
1 5 10 15
Gln Phe His Ile Asp Tyr Asn Asn Val Ser Ser Ala Glu Gly Trp His
20 25 30
Val Asn

<210> 195
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:C4BP-BINDING
PEPTIDE

<400> 195
Ser Gly Ile Ala Gln Phe His Ile Asp Tyr Asn Asn Val Ser
1 5 10

<210> 196
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 196
Ala Glu Pro Met Pro His Ser Leu Asn Phe Ser Gln Tyr Leu Trp Tyr

1 5 10 15

Thr

<210> 197

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 197

Ala Glu His Thr Tyr Ser Ser Leu Trp Asp Thr Tyr Ser Pro Leu Ala
1 5 10 15

Phe

<210> 198

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence:VINCULIN-BINDING PEPTIDE

<400> 198

Ala Glu Leu Asp Leu Trp Met Arg His Tyr Pro Leu Ser Phe Ser Asn
1 5 10 15

Arg

<210> 199

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 199

Ala Glu Ser Ser Leu Trp Thr Arg Tyr Ala Trp Pro Ser Met Pro Ser
1 5 10 15

Tyr

<210> 200

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 200

Ala Glu Trp His Pro Gly Leu Ser Phe Gly Ser Tyr Leu Trp Ser Lys
1 5 10 15

Thr

<210> 201

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 201

Ala Glu Pro Ala Leu Leu Asn Trp Ser Phe Phe Phe Asn Pro Gly Leu
1 5 10 15

His

<210> 202
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 202
Ala Glu Trp Ser Phe Tyr Asn Leu His Leu Pro Glu Pro Gln Thr Ile
1 5 10 15

Phe

<210> 203
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 203
Ala Glu Pro Leu Asp Leu Trp Ser Leu Tyr Ser Leu Pro Pro Leu Ala
1 5 10 15

Met

<210> 204
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 204
Ala Glu Pro Thr Leu Trp Gln Leu Tyr Gln Phe Pro Leu Arg Leu Ser

1 5 10 15

Gly

<210> 205

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 205

Ala Glu Ile Ser Phe Ser Glu Leu Met Trp Leu Arg Ser Thr Pro Ala
1 5 10 15

Phe

<210> 206

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 206

Ala Glu Leu Ser Glu Ala Asp Leu Trp Thr Thr Trp Phe Gly Met Gly
1 5 10 15

Ser

<210> 207

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 207

Ala Glu Ser Ser Leu Trp Arg Ile Phe Ser Pro Ser Ala Leu Met Met
1 5 10 15

Ser

<210> 208

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 208

Ala Glu Ser Leu Pro Thr Leu Thr Ser Ile Leu Trp Gly Lys Glu Ser
1 5 10 15

Val

<210> 209

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 209

Ala Glu Thr Leu Phe Met Asp Leu Trp His Asp Lys His Ile Leu Leu
1 5 10 15

Thr

<210> 210
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 210
Ala Glu Ile Leu Asn Phe Pro Leu Trp His Glu Pro Leu Trp Ser Thr
1 5 10 15
Glu

<210> 211
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 211
Ala Glu Ser Gln Thr Gly Thr Leu Asn Thr Leu Phe Trp Asn Thr Leu
1 5 10 15
Arg

<210> 212
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 1, Xaa is V, L, I, E, P, G, Y, M, T,

or D

<220>

<223> At position 2, Xaa is Y, W or F

<220>

<223> At position 3, Xaa is E, F, V, W or Y

<220>

<223> At position 5, Xaa is P or azetidine

<220>

<223> At position 7, Xaa is S, A, V or L

<220>

<223> At position 8, Xaa is M, F, V, R, Q, K, T, S, D,
L, I or E

<220>

<223> At position 9, Xaa is E, L, W, V, H, I, G, A, D,
L, Y, N, Q or P

<400> 212

Xaa Xaa Xaa Gln Xaa Tyr Xaa Xaa Xaa

1

5

<210> 213

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: IL-1 ANTAGONIST
PEPTIDE

<400> 213

Thr Ala Asn Val Ser Ser Phe Glu Trp Thr Pro Tyr Tyr Trp Gln Pro

1

5

10

15

Tyr Ala Leu Pro Leu

20

<210> 214

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 214

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Trp | Thr | Asp | Tyr | Gly | Tyr | Trp | Gln | Pro | Tyr | Ala | Leu | Pro | Ile | Ser |
| 1 | | | | | 5 | | | 10 | | | | | 15 | | |

Gly Leu

<210> 215

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 215

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Glu | Thr | Pro | Phe | Thr | Trp | Glu | Glu | Ser | Asn | Ala | Tyr | Tyr | Trp | Gln | Pro |
| 1 | | | | 5 | | | | 10 | | | | | | 15 | |

| | | | | |
|-----|-----|-----|-----|-----|
| Tyr | Ala | Leu | Pro | Leu |
| | | | 20 | |

<210> 216

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 216

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Glu | Asn | Thr | Tyr | Ser | Pro | Asn | Trp | Ala | Asp | Ser | Met | Tyr | Trp | Gln | Pro |
| 1 | | | | | 5 | | | | 10 | | | | | 15 | |

Tyr Ala Leu Pro Leu

20

<210> 217

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 217

Ser Val Gly Glu Asp His Asn Phe Trp Thr Ser Glu Tyr Trp Gln Pro
1 5 10 15Tyr Ala Leu Pro Leu
20

<210> 218

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 218

Asp Gly Tyr Asp Arg Trp Arg Gln Ser Gly Glu Arg Tyr Trp Gln Pro
1 5 10 15Tyr Ala Leu Pro Leu
20

<210> 219

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 219

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro Tyr
1 5 10

<210> 220

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 220

Phe Glu Trp Thr Pro Gly Tyr Trp Gln His Tyr
1 5 10

<210> 221

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa=azetidine

<400> 221

Phe Glu Trp Thr Pro Gly Trp Tyr Gln Xaa Tyr
1 5 10

<210> 222

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, optionally acetylated at N-terminus

<220>

<223> At position 10, Xaa=azetidine

<400> 222

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Trp | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 223

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 11, Xaa=azetidine

<400> 223

| | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Trp | Pro | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | | |

<210> 224

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa=azetidine

<400> 224

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Ala | Trp | Thr | Pro | Gly | Tyr | Trp | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 225
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 10, Xaa=azetidine

<400> 225
Phe Glu Trp Ala Pro Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 226
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 10, Xaa=azetidine

<400> 226
Phe Glu Trp Val Pro Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 227
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 10, Xaa=azetidine

<400> 227

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 228

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, optionally acetylated at N-terminus

<220>

<223> At position 10, Xaa=azetidine

<400> 228

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 229

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 6, products="MeGly"

<220>

<223> At position 10, Xaa=azetidine

<400> 229

Phe Glu Trp Thr Pro Xaa Trp Tyr Gln Xaa Tyr
1 5 10

<210> 230

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 6, Xaa=MeGly

<220>

<223> At position 10, Xaa=azetidine

<400> 230

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Xaa | Trp | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 231

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 231

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Tyr | Tyr | Gln | Pro | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 232

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 232

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Trp | Trp | Gln | Pro | Tyr |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|

1 5 10

<210> 233

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 233

Phe Glu Trp Thr Pro Asn Tyr Trp Gln Pro Tyr

1 5 10

<210> 234

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, Xaa=pipecolic acid

<220>

<223> At position 10, Xaa=azetidine

<400> 234

Phe Glu Trp Thr Xaa Val Tyr Trp Gln Xaa Tyr

1 5 10

<210> 235

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, Xaa=pipecolic acid

<220>

<223> At position 10, Xaa=azetidine

<400> 235

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Xaa | Gly | Tyr | Trp | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 236

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 6, Xaa=Aib

<220>

<223> At position 10, Xaa=azetidine

<400> 236

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Xaa | Tyr | Trp | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 237

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, Xaa=MeGly

<220>

<223> At position 10, Xaa=azetidine

<400> 237

Phe Glu Trp Thr Xaa Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 238

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 11, amino group added at C-terminus

<400> 238.

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro Tyr
1 5 10

<210> 239

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 11, amino group added at C-terminus

<400> 239

Phe Glu Trp Thr Pro Gly Tyr Trp Gln His Tyr
1 5 10

<210> 240

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11 amino group added at C-terminus

<400> 240

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Trp | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 241

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, optionally acetylated at
N-terminus

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11 amino group added at C-terminus

<400> 241

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Trp | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 242

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST

PEPTIDE

<220>

<223> At position 8, Xaa is a phyosphotyrosyl residue

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11, amino group added at C-terminus

<400> 242

Phe Glu Trp Thr Pro Gly Trp Xaa Gln Xaa Tyr

1

5

10

<210> 243

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11 amino group added at C-terminus

<400> 243

Phe Ala Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr

1

5

10

<210> 244

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11 amino group added at C-terminus

<400> 244

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Ala | Pro | Gly | Tyr | Trp | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 245

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11 amino group added at C-terminus

<400> 245

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Val | Pro | Gly | Tyr | Trp | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 246

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11 amino group added at C-terminus

<400> 246

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 247

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1 acetylated at N-terminus

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11 amino group added at C-terminus

<400> 247

Xaa Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 248

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 6, D amino acid residue

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11 amino group added at C-terminus

<400> 248

Phe Glu Trp Thr Pro Ala Trp Tyr Gln Xaa Tyr
1 5 10

<210> 249

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 6, Xaa is a sarcosine residue

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11 amino group added at C-terminus

<400> 249

Phe Glu Trp Thr Pro Xaa Trp Tyr Gln Xaa Tyr
1 5 10

<210> 250

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 11 amino group added at C-terminus

<400> 250

Phe Glu Trp Thr Pro Gly Tyr Tyr Gln Pro Tyr
1 5 10

<210> 251

<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 11 amino group added at C-terminus

<400> 251
Phe Glu Trp Thr Pro Gly Trp Trp Gln Pro Tyr
1 5 10

<210> 252
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 11 amino group added at C-terminus

<400> 252
Phe Glu Trp Thr Pro Asn Tyr Trp Gln Pro Tyr
1 5 10

<210> 253
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 6, D amino acid residue

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11, amino group added at C-terminus

<400> 253

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Val | Tyr | Trp | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 254

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, Xaa is a pipecolic acid residue

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11, amino group added at C-terminus

<400> 254

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Xaa | Gly | Tyr | Trp | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 255

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 6, Xaa=pipecolic acid

<220>

<223> At position 10, Xaa=azetidine

<400> 255

Phe Glu Trp Thr Pro Xaa Tyr Trp Gln Xaa Tyr
1 5 10

<210> 256

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, Xaa=MeGly

<220>

<223> At position 10, Xaa=azetidine

<400> 256

Phe Glu Trp Thr Xaa Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 257

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 257

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 258

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa is a 1-naphthylalanine residue

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11, amino group added at C-terminus

<400> 258

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Xaa | Glu | Trp | Thr | Pro | Gly | Tyr | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 259

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is a azetidine residue

<220>

<223> At position 11, amino group added at C-terminus

<400> 259

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Tyr | Glu | Trp | Thr | Pro | Gly | Tyr | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 260

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST

PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11, amino group added at C-terminus

<400> 260

Phe Glu Trp Val Pro Gly Tyr Tyr Gln Xaa Tyr

1

5

10

<210> 261

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 6, D amino acid residue

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11, amino group added at C-terminus

<400> 261

Phe Glu Trp Thr Pro Ser Tyr Tyr Gln Xaa Tyr

1

5

10

<210> 262

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 6, D amino acid residue

<220>

<223> At position 10, Xaa is an azetidine residue

<220>

<223> At position 11, amino group added at C-terminus

<400> 262

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Asn | Tyr | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 263

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 263

| | | | |
|-----|-----|-----|-----|
| Thr | Lys | Pro | Arg |
| 1 | | | |

<210> 264

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 264

| | | | | |
|-----|-----|-----|-----|-----|
| Arg | Lys | Ser | Ser | Lys |
| 1 | | | | 5 |

<210> 265

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 265

Arg Lys Gln Asp Lys
1 5

<210> 266

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 266

Asn Arg Lys Gln Asp Lys
1 5

<210> 267

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 267

Arg Lys Gln Asp Lys Arg
1 5

<210> 268

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST

PEPTIDE

<400> 268

Glu Asn Arg Lys Gln Asp Lys Arg Phe

1

5

<210> 269

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST

PEPTIDE

<400> 269

Val Thr Lys Phe Tyr Phe

1

5

<210> 270

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST

PEPTIDE

<400> 270

Val Thr Lys Phe Tyr

1

5

<210> 271

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST

PEPTIDE

<400> 271

Val Thr Asp Phe Tyr
1 5

<210> 272
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 272
Ser Gly Ser Gly Val Leu Lys Arg Pro Leu Pro Ile Leu Pro Val Thr
1 5 10 15

Arg

<210> 273
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MCA/MCP
PROTEASE INHIBITOR PEPTIDE

<400> 273
Arg Trp Leu Ser Ser Arg Pro Leu Pro Pro Leu Pro Leu Pro Pro Arg
1 5 10 15

Thr

<210> 274
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MCA/MCPPROTEASE

INHIBITOR PEPTIDE

<400> 274

Gly Ser Gly Ser Tyr Asp Thr Leu Ala Leu Pro Ser Leu Pro Leu His
1 5 10 15

Pro Met Ser Ser
20

<210> 275

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MCA/MCP
PROTEASE INHIBITOR PEPTIDE

<400> 275

Gly Ser Gly Ser Tyr Asp Thr Arg Ala Leu Pro Ser Leu Pro Leu His
1 5 10 15

Pro Met Ser Ser
20

<210> 276

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MCA/MCP
PROTEASE INHIBITOR PEPTIDE

<400> 276

Gly Ser Gly Ser Ser Gly Val Thr Met Tyr Pro Lys Leu Pro Pro His
1 5 10 15

Trp Ser Met Ala
20

<210> 277

<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MCA/MCP
PROTEASE INHIBITOR PEPTIDE

<400> 277
Gly Ser Gly Ser Ser Gly Val Arg Met Tyr Pro Lys Leu Pro Pro His
1 5 10 15

Trp Ser Met Ala
20

<210> 278
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MCA/MCP
PROTEASE INHIBITOR PEPTIDE

<400> 278
Gly Ser Gly Ser Ser Ser Met Arg Met Val Pro Thr Ile Pro Gly Ser
1 5 10 15

Ala Lys His Gly
20

<210> 279
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:ANTI-HBV
PEPTIDE

<400> 279
Leu Leu Gly Arg Met Lys
1 5

<210> 280

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:ANTI-HBV
PEPTIDE

<400> 280

Ala Leu Leu Gly Arg Met Lys Gly

1

5

<210> 281

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:ANTI-HBV
PEPTIDE

<400> 281

Leu Asp Pro Ala Phe Arg

1

5

<210> 282

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 282

Arg Pro Leu Pro Pro Leu Pro

1

5

<210> 283

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 283

Arg Glu Leu Pro Pro Leu Pro

1

5

<210> 284

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MSH3 ANTAGONIST

<400> 284

Ser Pro Leu Pro Pro Leu Pro

1

5

<210> 285

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 285

Gly Pro Leu Pro Pro Leu Pro

1

5

<210> 286

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 286

Arg Pro Leu Pro Ile Pro Pro

1

5

<210> 287

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MAST CELL
ANTAGONISTS/MAST CELL PROTEASE INHIBITOR

<400> 287

Arg Pro Leu Pro Ile Pro Pro

1

5

<210> 288

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 288

Arg Arg Leu Pro Pro Thr Pro

1

5

<210> 289

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 289

Arg Gln Leu Pro Pro Thr Pro

1

5

<210> 290
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 290
Arg Pro Leu Pro Ser Arg Pro
1 5

<210> 291
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 291
Arg Pro Leu Pro Thr Arg Pro
1 5

<210> 292
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 292
Ser Arg Leu Pro Pro Leu Pro
1 5

<210> 293
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 293

Arg Ala Leu Pro Ser Pro Pro

1

5

<210> 294

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 294

Arg Arg Leu Pro Arg Thr Pro

1

5

<210> 295

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 295

Arg Pro Val Pro Pro Ile Thr

1

5

<210> 296

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 296...

Ile Leu Ala Pro Pro Val Pro

1

5

<210> 297
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 297
Arg Pro Leu Pro Met Leu Pro
1 5

<210> 298
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 298
Arg Pro Leu Pro Ile Leu Pro
1 5

<210> 299
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 299
Arg Pro Leu Pro Ser Leu Pro
1 5

<210> 300
<211> 7
<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 300

Arg Pro Leu Pro Ser Leu Pro

1 5

<210> 301

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 301

Arg Pro Leu Pro Met Ile Pro

1 5

<210> 302

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 302

Arg Pro Leu Pro Leu Ile Pro

1 5

<210> 303

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 303

Arg Pro Leu Pro Pro Thr Pro
1 5

<210> 304

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 304

Arg Ser Leu Pro Pro Leu Pro
1 5

<210> 305

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 305

Arg Pro Gln Pro Pro Pro Pro
1 5

<210> 306

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 306

Arg Gln Leu Pro Ile Pro Pro
1 5

<210> 307

<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 307
Xaa Xaa Xaa Arg Pro Leu Pro Pro Leu Pro Xaa Pro
1 5 10

<210> 308
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 308
Xaa Xaa Xaa Arg Pro Leu Pro Pro Ile Pro Xaa Xaa
1 5 10

<210> 309
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 309
Xaa Xaa Xaa Arg Pro Leu Pro Pro Leu Pro Xaa Xaa
1 5 10

<210> 310
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 310

Arg Xaa Xaa Arg Pro Leu Pro Pro Leu Pro Xaa Pro
1 5 10

<210> 311

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 311

Arg Xaa Xaa Arg Pro Leu Pro Pro Leu Pro Pro Pro
1 5 10

<210> 312

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 312

Pro Pro Pro Tyr Pro Pro Pro Pro Ile Pro Xaa Xaa
1 5 10

<210> 313

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 313

Pro Pro Pro Tyr Pro Pro Pro Pro Val Pro Xaa Xaa
1 5 10

<210> 314
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 314
Leu Xaa Xaa Arg Pro Leu Pro Xaa Xaa Pro
1 5 10

<210> 315
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<220>
<223> At position 1, Xaa is an aliphatic amino acid
residue

<400> 315
Xaa Xaa Xaa Arg Pro Leu Pro Xaa Leu Pro
1 5 10

<210> 316
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:SH3 ANTAGONIST

<220>
<223> At position 4, Xaa is an aromatic amino acid
residue

<220>
<223> At position 9, Xaa is an aliphatic amino acid
residue

<400> 316

Pro Pro Xaa Xaa Tyr Pro Pro Pro Xaa Pro
1 5 10

<210> 317

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<220>

<223> At position 1, Xaa is a basic amino acid residue

<220>

<223> At position 4, Xaa is an aliphatic amino acid
residue

<400> 317

Xaa Pro Pro Xaa Pro Xaa Lys Pro Xaa Trp Leu
1 5 10

<210> 318

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<220>

<223> At position 4, Xaa is an aliphatic amino acid
residue

<220>

<223> At position 6, Xaa is an aliphatic amino acid
residue

<220>

<223> At position 8, Xaa is a basic amino acid residue

<400> 318

Arg Pro Xaa Xaa Pro Xaa Arg Xaa Ser Xaa Pro
1 5 10

<210> 319

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 319

Pro Pro Val Pro Pro Arg Pro Xaa Xaa Thr Leu
1 5 10

<210> 320

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<220>

<223> At positions 1, 3 and 6, Xaa is an aliphatic
amino acid residue

<400> 320

Xaa Pro Xaa Leu Pro Xaa Lys
1 5

<210> 321

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<220>

<223> At position 1, Xaa is a basic amino acid residue

<220>

<223> At position 2, Xaa is an aromatic amino acid
residue

<400> 321

Xaa Xaa Asp Xaa Pro Leu Pro Xaa Leu Pro
1 5 10

<210> 322

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INHIBITOR OF
PLATELET AGGREGATION

<400> 322

Cys Xaa Xaa Arg Gly Asp Cys
1 5

<210> 323

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SRC ANTAGONIST

<400> 323

Arg Pro Leu Pro Pro Leu Pro
1 5

<210> 324

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SRC ANTAGONIST

<400> 324

Pro Pro Val Pro Pro Arg
1 5

<210> 325
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:ANTI-CANCER
PEPTIDE

<400> 325
Xaa Phe Xaa Asp Xaa Trp Xaa Xaa Leu Xaa Xaa
1 5 10

<210> 326
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:p16-MIMETIC
PEPTIDE

<400> 326
Lys Ala Cys Arg Arg Leu Phe Gly Pro Val Asp Ser Glu Gln Leu Ser
1 5 10 15

Arg Asp Cys Asp
20

<210> 327
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:p16-MIMETIC
PEPTIDE

<400> 327

Arg Glu Arg Trp Asn Phe Asp Phe Val Thr Glu Thr Pro Leu Glu Gly
1 5 10 15

Asp Phe Ala Trp
20

<210> 328

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:p16-MIMETIC
PEPTIDE

<400> 328

Lys Arg Arg Gln Thr Ser Met Thr Asp Phe Tyr His Ser Lys Arg Arg
1 5 10 15

Leu Ile Phe Ser
20

<210> 329

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SH3 ANTAGONIST

<400> 329

Thr Ser Met Thr Asp Phe Tyr His Ser Lys Arg Arg Leu Ile Phe Ser
1 5 10 15

Lys Arg Lys Pro
20

<210> 330

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:p16-MIMETIC
PEPTIDE

<400> 330

Arg Arg Leu Ile Phe
1 5

<210> 331

<211> 36

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:p16-MIMETIC
PEPTIDE

<400> 331

Lys Arg Arg Gln Thr Ser Ala Thr Asp Phe Tyr His Ser Lys Arg Arg
1 5 10 15Leu Ile Phe Ser Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met
20 25 30Lys Trp Lys Lys
35

<210> 332

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:p16-MIMETIC
PEPTIDE

<400> 332

Lys Arg Arg Leu Ile Phe Ser Lys Arg Gln Ile Lys Ile Trp Phe Gln
1 5 10 15Asn Arg Arg Met Lys Trp Lys Lys
20

<210> 333
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:POLYGLYCINE
LINKER

<400> 333
Gly Gly Gly Lys Gly Gly Gly Gly
1 5

<210> 334
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:POLYGLYCINE
LINKER

<400> 334
Gly Gly Gly Asn Gly Ser Gly Gly
1 5

<210> 335
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:POLYGLYCINE
LINKER

<400> 335
Gly Gly Gly Cys Gly Gly Gly Gly
1 5

<210> 336
<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:FC PCR PRIMER

<400> 336

Gly Pro Asn Gly Gly
1 5

<210> 337

<211> 42

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC

<400> 337

Phe Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu
1 5 10 15

Ala Ala Arg Ala Gly Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro
20 25 30

Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
35 40

<210> 338

<211> 42

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC

<400> 338

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
1 5 10 15

Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu
20 25 30

Ala Ala Arg Ala Gly Gly Gly Gly Gly Phe

35

40

<210> 339

<211> 50

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC

<400> 339

Phe Gly Gly Gly Gly Gly Gly Gly Thr Tyr Ser Cys His Phe Gly Pro
 1 5 10 15

Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Gly Gly Gly Gly Gly Gly
 20 25 30

Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys Pro Gln
 35 40 45

Gly Gly
 50

<210> 340

<211> 50

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC

<400> 340

Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
 1 5 10 15

Pro Gln Gly Gly Gly Gly Gly Gly Gly Gly Thr Tyr Ser Cys His Phe
 20 25 30

Gly Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Gly Gly Gly Gly Gly
 35 40 45

Gly Phe
 50

<210> 341

<211> 28

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDES

<400> 341

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Ile Glu
1 5 10 15

Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
20 25

<210> 342

<211> 29

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC

<400> 342

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Ile
1 5 10 15

Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
20 25

<210> 343

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC

<400> 343

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
1 5 10 15

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
 20 25 30

<210> 344

<211> 31

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC

<400> 344

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
 1 5 10 15

Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
 20 25 30

<210> 345

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC

<400> 345

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
 1 5 10 15

Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
 20 25 30

<210> 346

<211> 33

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC

<400> 346

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Glu | Gly | Pro | Thr | Leu | Arg | Gln | Trp | Leu | Ala | Ala | Arg | Ala | Gly | Gly |
| 1 | | | | | 5 | | | | 10 | | | | | 15 | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Gly | Gly | Ile | Glu | Gly | Pro | Thr | Leu | Arg | Gln | Trp | Leu | Ala | Ala | Arg |
| | | | 20 | | | | | 25 | | | | | 30 | | |

Ala

<210> 347

<211> 34

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC

<400> 347

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Glu | Gly | Pro | Thr | Leu | Arg | Gln | Trp | Leu | Ala | Ala | Arg | Ala | Gly | Gly |
| 1 | | | | | 5 | | | | 10 | | | | | 15 | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Gly | Gly | Gly | Ile | Glu | Gly | Pro | Thr | Leu | Arg | Gln | Trp | Leu | Ala | Ala |
| | | | | 20 | | | | | 25 | | | | | 30 | |

Arg Ala

<210> 348

<211> 35

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC

<400> 348

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Glu | Gly | Pro | Thr | Leu | Arg | Gln | Trp | Leu | Ala | Ala | Arg | Ala | Gly | Gly |
| 1 | | | | | 5 | | | | 10 | | | | | 15 | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Gly | Gly | Gly | Gly | Ile | Glu | Gly | Pro | Thr | Leu | Arg | Gln | Trp | Leu | Ala |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|

20

25

30

Ala Arg Ala
35

<210> 349

<211> 36

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC

<400> 349

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
1 5 10 15

Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu
20 25 30

Ala Ala Arg Ala
35

<210> 350

<211> 37

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDES

<400> 350

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
1 5 10 15

Gly Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp
20 25 30

Leu Ala Ala Arg Ala
35

<210> 351
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:TPO-MIMETIC
 PEPTIDES

<400> 351
 Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
 1 5 10 15
 Gly Gly Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln
 20 25 30
 Trp Leu Ala Ala Arg Ala
 35

<210> 352
 <211> 42
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:TPO-MIMETIC
 PEPTIDES

<400> 352
 Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
 1 5 10 15
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro
 20 25 30
 Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
 35 40

<210> 353
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDES

<400> 353

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Pro
1 5 10 15

Asn Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
20 25 30

<210> 354

<211> 36

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDES

<400> 354

Ile Glu Gly Pro Thr Leu Arg Gln Cys Leu Ala Ala Arg Ala Gly Gly
1 5 10 15

Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Cys Leu
20 25 30

Ala Ala Arg Ala
35

<210> 355

<211> 36

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDES

<400> 355

Ile Glu Gly Pro Thr Leu Arg Gln Cys Leu Ala Ala Arg Ala Gly Gly
1 5 10 15

Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Cys Leu
 20 25 30

Ala Ala Arg Ala
 35

<210> 356

<211> 36

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
 PEPTIDES

<400> 356

Ile Glu Gly Pro Thr Leu Arg Gln Ala Leu Ala Ala Arg Ala Gly Gly
 1 5 10 15

Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Ala Leu
 20 25 30

Ala Ala Arg Ala
 35

<210> 357

<211> 36

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
 PEPTIDES

<400> 357

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
 1 5 10 15

Gly Lys Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu
 20 25 30

Ala Ala Arg Ala
 35

<210> 358
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDES

<400> 358
Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
1 5 10 15
Gly Lys Asx Arg Ala Cys Gly Gly Gly Ile Glu Gly Pro Thr Leu
20 25 30
Arg Gln Trp Leu Ala Ala Arg Ala
35 40

<210> 359
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDES

<400> 359
Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
1 5 10 15
Gly Cys Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu
20 25 30
Ala Ala Arg Ala
35

<210> 360
<211> 39
<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDES

<400> 360

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
1 5 10 15

Gly Lys Pro Glu Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg
20 25 30

Gln Trp Leu Ala Ala Arg Ala
35

<210> 361

<211> 39

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDES

<400> 361

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
1 5 10 15

Gly Cys Pro Glu Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg
20 25 30

Gln Trp Leu Ala Ala Arg Ala
35

<210> 362

<211> 36

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
PEPTIDES

<400> 362

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
 1 5 10 15

Gly Asn Gly Ser Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu
 20 25 30

Ala Ala Arg Ala
 35

<210> 363

<211> 36

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO-MIMETIC
 PEPTIDES

<400> 363

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly
 1 5 10 15

Gly Cys Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu
 20 25 30

Ala Ala Arg Ala
 35

<210> 364

<211> 57

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TMP PCR
 PRIMER

<400> 364

aaaaaaggat cctcgagatt aagcacgagc agccagccac tgacgcagag tcggacc 57

<210> 365

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TMP PCR
PRIMER

<400> 365

aaaggtggag gtggtggtat cgaaggtccg actctgcgt

39

<210> 366

<211> 42

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 366

cagtggctgg ctgctcgtgc ttaatctcga ggatcctttt tt

42

<210> 367

<211> 81

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TMP

<400> 367

aaaggtggag gtggtggtat cgaaggtccg actctgcgtc agtggctggc tgctcgtgct 60
taatctcgag gatccttttt t 81

<210> 368

<211> 52

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TMP

<400> 368

ttcgatacca ccacctccac ctttaccgg agacaggag aggtcttct gc

52

<210> 369
<211> 60
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Fc-TMP-TMP

<400> 369
aaaggtggag gtggtggtat cgaaggtccg actctgcgtc agtggctggc tgctcgtgct 60

<210> 370
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:FC PCR PRIMER

<400> 370
acctccacca ccagcacgag cagccagcca ctgacgcaga gtcggacc 48

<210> 371
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Fc-TMP-TMP
OLIGONUCLEOTIDE

<400> 371
ggtggtggag gtggcggcgg aggtattgag ggcccaaccc ttcgccaatg gcttgacgca 60
cgcgca 66

<210> 372
<211> 76
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Fc-TMP-TMP
OLIGONUCLEOTIDE

<400> 372

aaaaaaagga tcctcgagat tatgcgcgtg ctgcaagcca ttggcgaagg gttgggccct 60
 caatacctcc gccgcc 76

<210> 373

<211> 126

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TNF ALPHA
 PCR PRIMER

<220>

<221> CDS

<222> (1)..(126)

<400> 373

aaa ggt gga ggt ggt ggt atc gaa ggt ccg act ctg cgt cag tgg ctg 48
 Lys Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu
 1 5 10 15

gct gct cgt gct ggt ggt gga ggt ggc ggc gga ggt att gag ggc cca 96
 Ala Ala Arg Ala Gly Gly Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro
 20 25 30

acc ctt cgc caa tgg ctt gca gca cgc gca 126
 Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
 35 40

<210> 374

<211> 42

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc-TNF ALPHA
 PCR PRIMER

<400> 374

Lys Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu
 1 5 10 15

Ala Ala Arg Ala Gly Gly Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro
 20 25 30

Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala
 35 40

<210> 375
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Fc-MMP
INHIBITOR

<220>
<221> CDS
<222> (4)..(732)

<400> 375
ttt ttt cat atg atc gaa ggt ccg act ctg cgt cag tgg
Phe His Met Ile Glu Gly Pro Thr Leu Arg Gln Trp
1 5 10

39

<210> 376
<211> 12
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence:Fc-MMP
INHIBITOR

<400> 376
Phe His Met Ile Glu Gly Pro Thr Leu Arg Gln Trp
1 5 10

<210> 377
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MMP INHIBITOR
Fc

<220>
<221> CDS
<222> (4)..(753)

<400> 377

agc acg agc agc cag cca ctg acg cag agt cgg acc ttc gat cat atg 48
 Thr Ser Ser Gln Pro Leu Thr Gln Ser Arg Thr Phe Asp His Met
 1 5 10 15

<210> 378

<211> 15

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:MMP INHIBITOR
 Fc

<400> 378

Thr Ser Ser Gln Pro Leu Thr Gln Ser Arg Thr Phe Asp His Met
 1 5 10 15

<210> 379

<211> 45

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TMP-TMP-Fc
 OLIGONUCLEOTIDE

<400> 379

ctggctgctc gtgctggtgg aggcggtggg gacaaaactc acaca 45

<210> 380

<211> 51

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
 BINDING PEPTIDE

<400> 380

ctggctgctc gtgctggcgg tggcggcgga ggggggtggca ttgagggccc a 51

<210> 381

<211> 54

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 381

aagccattgg cgaagggttg ggcctcaat gccacccct ccgccaccac cgcc 54

<210> 382

<211> 54

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 382

acccttcgcc aatggcttgc agcacgcgca gggggaggcg gtggggacaa aact 54

<210> 383

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 383

cccaccgcct cccctgcgc gtgctgc 27

<210> 384

<211> 189

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<220>

<221> CDS

<222> (10)..(189)

<400> 384

ttttttcat atg atc gaa ggt ccg act ctg cgt cag tgg ctg gct gct cgt 51

Met Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg

1

5

10

gct ggc ggt ggt ggc gga ggg ggt ggc att gag ggc cca acc ctt cgc 99

Ala Gly Gly Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg

15

20

25

30

caa tgg ctg gct gct cgt gct ggt gga ggc ggt ggg gac aaa act ctg 147

Gln Trp Leu Ala Ala Arg Ala Gly Gly Gly Gly Gly Gly Asp Lys Thr Leu

35

40

45

gct gct cgt gct ggt gga ggc ggt ggg gac aaa act cac aca 189

Ala Ala Arg Ala Gly Gly Gly Gly Gly Gly Asp Lys Thr His Thr

50

55

60

<210> 385

<211> 60

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:INTEGRIN

BINDING PEPTIDE

<400> 385

Met Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly

1

5

10

15

Gly Gly Gly Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp

20

25

30

Leu Ala Ala Arg Ala Gly Gly Gly Gly Gly Gly Asp Lys Thr Leu Ala Ala

35

40

45

Arg Ala Gly Gly Gly Gly Gly Gly Asp Lys Thr His Thr

50

55

60

<210> 386

<211> 141

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN

BINDING PEPTIDE

<400> 386

ctaattccgc tctcacctac caaacaatgc ccccctgcaa aaaataaatt catataaaaa 60
 acatacagat aaccatctgc ggtgataaat tatctctggc ggtggtgaca taaataccac 120
 tggcggatgat actgagcaca t 141

<210> 387

<211> 55

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
 BINDING PEPTIDE

<400> 387

cgatttgatt ctagaaggag gaataacata tgggtaacgc gttggaattc ggtac 55

<210> 388

<211> 872

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
 BINDING PEPTIDE

<400> 388

ttattttcgt gcggccgcac cattatcacc gccagaggta aactagtcaa cacgcacggt 60
 gttagatatt tatcccttgc ggtgatagat tgagcacatc gatttgattc tagaaggagg 120
 gataatatat gagcacaaaa aagaaacat taacacaaga gcagcttgag gacgcacgtc 180
 gccttaaagc aatttatgaa aaaaagaaaa atgaacttgg cttatcccag gaatctgtcg 240
 cagacaagat ggggatgggg cagtcaggcg ttggtgcttt atttaatggc atcaatgcat 300
 taaatgctta taacgccgca ttgcttacia aaattctcaa agttagcgtt gaagaattta 360
 gcccttcaat cgccagagaa tctacgagat gtatgaagcg gttagtatgc agccgtcact 420
 tagaagttag tatgagtacc ctgttttttc tcatgttcag gcagggatgt tctcacctaa 480
 gcttagaacc ttaccaaaag gtgatgcgga gagatgggta agcacaacca aaaaagccag 540
 tgattctgca ttctggcttg aggttgaagg taattccatg accgcaccaa caggctccaa 600
 gccaaagcttt cctgacggaa tgtaattct cgttgacct gagcaggctg ttgagccagg 660
 tgatttctgc atagccagac ttgggggtga tgagtttacc ttcaagaaac tgatcaggga 720
 tagcggctag gtgtttttac aaccactaaa cccacagtac ccaatgatcc catgcaatga 780
 gagttgttcg gttgtgggga aagttatcgc tagtcagtgg cctgaagaga cgtttggctg 840
 atagactagt ggatccacta gtgtttctgc cc 872

<210> 389
 <211> 1197
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:INTEGRIN
 BINDING PEPTIDE

<400> 389
 ggcggaaacc gacgtccatc gaatgggtgca aaaccttttcg cggatatggca tgatagcgcc 60
 cggaagagag tcaattcagg gtgggtgaatg tgaaaccagt aacggtatac gatgtcgcag 120
 agtatgccgg tgtctcttat cagaccgttt cccgcgtggg gaaccaggcc agccacgttt 180
 ctgcgaaaac gcgggaaaaa gtcgaagcgg cgatggcgga gctgaattac attcccaacc 240
 gcgtggcaca acaactggcg ggcaaacagt cgctcctgat tggcgttgcc acctccagtc 300
 tggccctgca cgcgccgtcg caaattgtcg cggcgattaa atctcgcgcc gatcaactgg 360
 gtgccagcgt ggtgggtgtcg atggtagaac gaagcggcgt cgaagcctgt aaagcggcgg 420
 tgcacaatct tctcgcgcaa cgcgtcagtg ggctgatcat taactatccg ctggatgacc 480
 aggatgccat tgctgtggaa gctgcctgca ctaatgttcc ggcgttattt cttgatgtct 540
 ctgaccagac acccatcaac agtattattt tctcccatga agacgggtacg cgactgggcy 600
 tggagcatct ggtcgcattg ggtcaccagc aaatcgcgct gttagcgggc ccattaagtt 660
 ctgtctcggc gcgtctgcgt ctggctggct ggcataaata tctcactcgc aatcaaattc 720
 agccgatagc ggaacgggaa ggcgactgga gtgccatgtc cggttttcaa caaaccatgc 780
 aaatgctgaa tgagggcatc gttcccactg cgatgctggg tgccaacgat cagatggcgc 840
 tgggcgcaat gcgcgccatt accgagtcgg ggctgcgcgt tggcgcggat atctcggtag 900
 tgggatacga cgataccgaa gacagctcat gttatatccc gccgttaacc accatcaaac 960
 aggattttct cctgctgggg caaaccagcg tggaccgctt gctgcaactc tctcagggcc 1020
 aggcggtgaa gggcaatcag ctgttgcccg tctcactggg gaaaagaaaa accaccctgg 1080
 cgccaatac gcaaaccgcc tctcccgcgc cgttggccga ttcattaatg cagctggcac 1140
 gacaggtttc ccgactggaa agcggacagt aaggtaccat aggatccagg cacagga 1197

<210> 390
 <211> 61
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:Fc-EMP
 OLIGONUCLEOTIDE

<400> 390
 tatgaaaggt ggaggtgggt gtggaggtac ttactcttgc cacttcggcc cgctgacttg 60
 g 61

<210> 391
 <211> 72

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-EMP
OLIGONUCLEOTIDE

<400> 391

cggtttgcaa acccaagtca gcgggccgaa gtggcaagag taagtacctc caccaccacc 60
tccacctttc at 72

<210> 392

<211> 57

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-EMP
OLIGONUCLEOTIDE

<400> 392

gtttgcaaac cgcagggtgg cggcggcggc ggcggtggta cctattcctg tcatttt 57

<210> 393

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-EMP
OLIGONUCLEOTIDE

<400> 393

ccaggtcagc gggccaaaat gacaggaata ggtaccaccg ccgccgccgc cgccaccctg 60

<210> 394

<211> 118

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-EMP PCR
TEMPLATE

<220>

<221> CDS

<222> (2)..(118)

<400> 394

t atg aaa ggt gga ggt ggt ggt gga ggt act tac tct tgc cac ttc ggc 49

Met Lys Gly Gly Gly Gly Gly Gly Gly Thr Tyr Ser Cys His Phe Gly

1

5

10

15

ccg ctg act tgg gtt tgc aaa ccg cag ggt ggc ggc ggc ggc ggc ggt 97

Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Gly Gly Gly Gly Gly

20

25

30

ggt acc tat tcc tgt cat ttt

118

Gly Thr Tyr Ser Cys His Phe

35

<210> 395

<211> 39

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc-EMP PCR

TEMPLATE

<400> 395

Met Lys Gly Gly Gly Gly Gly Gly Gly Thr Tyr Ser Cys His Phe Gly

1

5

10

15

Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Gly Gly Gly Gly Gly

20

25

30

Gly Thr Tyr Ser Cys His Phe

35

<210> 396

<211> 61

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-EMP PCR

PRIMER

<400> 396

gcagaagagc ctctccctgt ctccgggtaa aggtggaggt ggtggtggag gtacttactc 60

t

61

<210> 397

<211> 40

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-EMP PCR
PRIMER

<400> 397

ctaattggat ccacgagatt aaccaccctg cggtttgcaa

40

<210> 398

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc PRIMER

<400> 398

aacataagta cctgtaggat cg

22

<210> 399

<211> 61

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc PRIMER

<400> 399

agagtaagta cctccaccac cacctccacc ttaccgga gacagggaga ggctcttctg 60
c 61

<210> 400

<211> 61

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-Fc
OLIGONUCLEOTIDE

<400> 400

ggcccgctga cctgggtatg taagccacaa ggggggtgggg gaggcggggg gtaatctoga 60
g 61

<210> 401

<211> 50

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-Fc
OLIGONUCLEOTIDE

<400> 401

gatactcgag attaccccc gcctcccca ccccttggtg gcttacatac 50

<210> 402

<211> 118

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-Fc PCR
TEMPLATE

<220>

<221> CDS

<222> (1)..(108)

<400> 402

ggt tgc aaa ccg cag ggt ggc ggc ggc ggc ggc ggt ggt acc tat tcc 48
Val Cys Lys Pro Gln Gly Gly Gly Gly Gly Gly Gly Thr Tyr Ser
1 5 10 15

tgt cat ttt ggc ccg ctg acc tgg gta tgt aag cca caa ggg ggt ggg 96
Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Gly
20 25 30

gga ggc ggg ggg taatctcgag 118
Gly Gly Gly Gly
35

<210> 403

<211> 36

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:EMP-Fc PCR
TEMPLATE

<400> 403

Val Cys Lys Pro Gln Gly Gly Gly Gly Gly Gly Gly Gly Thr Tyr Ser
1 5 10 15

Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Gly
20 25 30

Gly Gly Gly Gly
35

<210> 404

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-Fc PCR
PRIMER

<400> 404

ttatttcata tgaaagggtgg taactattcc tgtcatttt

39

<210> 405

<211> 43

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-Fc PCR
PRIMER

<400> 405

tggacatgtg tgagttttgt cccccccgcc tccccacccc cct

43

<210> 406

<211> 43

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc PRIMER

<400> 406

agggggtggg ggaggcggg gggacaaaac tcacacatgt cca

43

<210> 407

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc PRIMER

<400> 407

gttattgctc agcgggtggca

20

<210> 408

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-EMP-Fc
OLIGONUCLEOTIDE

<400> 408

ttttttatcg atttgattct agatttgagt tttaactttt agaaggagga ataaaatattg 60

<210> 409

<211> 41

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-EMP-Fc
OLIGONUCLEOTIDE

<400> 409

taaaagttaa aactcaaadc tagaatcaaa tcgataaaaa a

41

<210> 410

<211> 51

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-EMP-Fc
OLIGONUCLEOTIDE

<400> 410

ggaggtactt actcttgcca cttcggcccg ctgacttggg ttgcaaacc g 51

<210> 411

<211> 55

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-EMP-Fc
OLIGONUCLEOTIDE

<400> 411

agtcagcggg ccgaagtggc aagagtaagt acctcccata tttattcct ccttc 55

<210> 412

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-EMP-Fc
OLIGONUCLEOTIDE

<400> 412

caggggtggcg gcggcgggcg cggtggtacc tattcctgtc attttgccc gctgacctgg 60

<210> 413

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-EMP-Fc
OLIGONUCLEOTIDE

<400> 413

aaaatgacag gaataggtac caccgccgcc gccgccgcca ccctgcgggt tgcaaacc 60

<210> 414

<211> 57

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-EMP-Fc
OLIGONUCLEOTIDE

<400> 414

gtatgtaagc cacaaggggg tgggggagggc ggggggggaca aaactcacac atgtcca 57

<210> 415

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-EMP-Fc
OLIGONUCLEOTIDE

<400> 415

agttttgtcc cccccgcctc cccaccccc ttgtggctta cataccagcgcg tccagcgggcc 60

<210> 416

<211> 228

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EMP-EMP-Fc PCR
TEMPLATE

<220>

<221> CDS

<222> (58)..(228)

<400> 416

ttttttatcg atttgattct agatttgagt tttaactttt agaaggagga ataaaaat 57

atg gga ggt act tac tct tgc cac ttc ggc ccg ctg act tgg gtt tgc 105
Met Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys
1 5 10 15

aaa ccg cag ggt ggc ggc ggc ggc ggc ggt ggt acc tat tcc tgt cat 153

Lys Pro Gln Gly Gly Gly Gly Gly Gly Gly Gly Thr Tyr Ser Cys His
 20 25 30

ttt ggc ccg ctg acc tgg gta tgt aag cca caa ggg ggt ggg gga ggc 201
 Phe Gly Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Gly Gly Gly
 35 40 45

ggg ggg gac aaa act cac aca tgt cca 228
 Gly Gly Asp Lys Thr His Thr Cys Pro
 50 55

<210> 417

<211> 57

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:EMP-EMP-Fc PCR
 TEMPLATE

<400> 417

Met Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys
 1 5 10 15

Lys Pro Gln Gly Gly Gly Gly Gly Gly Gly Gly Thr Tyr Ser Cys His
 20 25 30

Phe Gly Pro Leu Thr Trp Val Cys Lys Pro Gln Gly Gly Gly Gly Gly
 35 40 45

Gly Gly Asp Lys Thr His Thr Cys Pro
 50 55

<210> 418

<211> 40

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-EMP-EMP PCR
 PRIMER

<400> 418

ctaattggat cctcgagatt aacccccttg tggcttacat 40

<210> 419

<211> 72

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 419

Xaa Tyr Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 1 5 10 15

Gly Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Thr Trp Xaa Xaa Xaa Xaa Xaa Xaa
 20 25 30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 35 40 45

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 50 55 60

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 65 70

<210> 420

<211> 62

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 420

Xaa Tyr Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Gly Pro
 1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Thr Trp Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys
 20 25 30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 35 40 45

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 50 55 60

<210> 421

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<220>

<223> At position 2, Xaa is R, H, L or W

<220>

<223> At position 3, Xaa is M, F or I

<220>

<223> At position 6, Xaa is any of the 20 genetically
encoded amino acid residues or a D-stereoisomer
thereof

<220>

<223> At position 9, Xaa is D, E, I, L or V

<400> 421

Cys Xaa Xaa Gly Pro Xaa Thr Trp Xaa Cys
1 5 10

<210> 422

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 422

Gly Gly Thr Tyr Ser Cys His Gly Pro Leu Thr Trp Val Cys Lys Pro
1 5 10 15

Gln Gly Gly

<210> 423

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 423

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Gly | Asn | Tyr | Met | Ala | His | Met | Gly | Pro | Ile | Thr | Trp | Val | Cys | Arg |
| 1 | | | | 5 | | | | 10 | | | | | 15 | | |

Pro Gly Gly

<210> 424

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 424

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Gly | Pro | His | His | Val | Tyr | Ala | Cys | Arg | Met | Gly | Pro | Leu | Thr | Trp |
| 1 | | | | 5 | | | | 10 | | | | | 15 | | |

Ile Cys

<210> 425

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 425

Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys

1 5 10 15

Pro Gln

<210> 426

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 426

Gly Gly Leu Tyr Ala Cys His Met Gly Pro Met Thr Trp Val Cys Gln
1 5 10 15

Pro Leu Arg Gly
20

<210> 427

<211> 22

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 427

Thr Ile Ala Gln Tyr Ile Cys Tyr Met Gly Pro Glu Thr Trp Glu Cys
1 5 10 15

Arg Pro Ser Pro Lys Ala
20

<210> 428

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 428

Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
1 5 10

<210> 429

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC
PEPTIDE

<400> 429

Tyr Cys His Phe Gly Pro Leu Thr Trp Val Cys
1 5 10

<210> 430

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 430

Ala Glu Pro Val Tyr Gln Tyr Glu Leu Asp Ser Tyr Leu Arg Ser Tyr
1 5 10 15

Tyr

<210> 431

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 431

Ala Glu Leu Asp Leu Ser Thr Phe Tyr Asp Ile Gln Tyr Leu Leu Arg
1 5 10 15

Thr

<210> 432

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 432

Ala Glu Phe Phe Lys Leu Gly Pro Asn Gly Tyr Val Tyr Leu His Ser
1 5 10 15

Ala

<210> 433

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 433

Phe Lys Leu Xaa Xaa Xaa Gly Tyr Val Tyr Leu
1 5 10

<210> 434

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 434

Ala Glu Ser Thr Tyr His His Leu Ser Leu Gly Tyr Met Tyr Thr Leu
1 5 10 15

Asn

<210> 435

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:UKR ANTAGONIST
PEPTIDE

<400> 435

Tyr His Xaa Leu Xaa Xaa Gly Tyr Met Tyr Thr
1 5 10

<210> 436

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MCA/MCP
INHIBITOR

<400> 436

Arg Asn Arg Gln Lys Thr
1 5

<210> 437

<211> 4

<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MCA/MCP
INHIBITOR

<400> 437
Arg Asn Arg Gln
1

<210> 438
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MCA/MCP
INHIBITOR

<400> 438
Arg Asn Arg Gln Lys
1 5

<210> 439
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MCA/MCP
INHIBITOR

<400> 439
Asn Arg Gln Lys Thr
1 5

<210> 440
<211> 4
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MCA/MCP
INHIBITOR

<400> 440

Arg Gln Lys Thr

1

<210> 441

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 441

Arg Xaa Glu Thr Xaa Trp Xaa

1

5

<210> 442

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 442

Arg Xaa Glu Thr Xaa Trp Xaa

1

5

<210> 443

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 443

Arg Gly Asp Gly Xaa

1 5

<210> 444

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial

Sequence:INTEGRIN-BINDING PEPTIDE

<400> 444

Cys Arg Gly Asp Gly Xaa Cys

1 5

<210> 445

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial

Sequence:INTEGRIN-BINDING PEPTIDE

<400> 445

Cys Xaa Xaa Arg Leu Asp Xaa Xaa Cys

1 5

<210> 446

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial

Sequence:INTEGRIN-BINDING PEPTIDE

<400> 446

Cys Ala Arg Arg Leu Asp Ala Pro Cys

1

5

<210> 447

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial

Sequence:INTEGRIN-BINDING PEPTIDE

<400> 447

Cys Pro Ser Arg Leu Asp Ser Pro Cys

1

5

<210> 448

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial

Sequence:INTEGRIN-BINDING PEPTIDE

<400> 448

Xaa Xaa Xaa Arg Gly Asp Xaa Xaa Xaa

1

5

<210> 449

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial

Sequence:INTEGRIN-BINDING PEPTIDE

<400> 449

Cys Xaa Cys Arg Gly Asp Cys Xaa Cys

1

5

<210> 450
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 450
Cys Asp Cys Arg Gly Asp Cys Phe Cys
1 5

<210> 451
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 451
Cys Asp Cys Arg Gly Asp Cys Leu Cys
1 5

<210> 452
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 452
Cys Leu Cys Arg Gly Asp Cys Ile Cys
1 5

<210> 453
<211> 8

<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 453
Xaa Xaa Asp Asp Xaa Xaa Xaa Xaa
1 5

<210> 454
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 454
Xaa Xaa Xaa Asp Asp Xaa Xaa Xaa Xaa Xaa
1 5 10

<210> 455
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 455
Cys Trp Asp Asp Gly Trp Leu Cys
1 5

<210> 456
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence: INTEGRIN-BINDING PEPTIDE

<400> 456

Cys Trp Asp Asp Leu Trp Trp Leu Cys
1 5

<210> 457

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence: INTEGRIN-BINDING PEPTIDE

<400> 457

Cys Trp Asp Asp Gly Leu Met Cys
1 5

<210> 458

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence: INTEGRIN-BINDING PEPTIDE

<400> 458

Cys Trp Asp Asp Gly Trp Met Cys
1 5

<210> 459

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence: INTEGRIN-BINDING PEPTIDE

<400> 459

Cys Ser Trp Asp Asp Gly Trp Leu Cys

1

5

<210> 460

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 460

Cys Pro Asp Asp Leu Trp Trp Leu Cys

1

5

<210> 461

<211> 40

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 461

Tyr Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Gly

1

5

10

15

Pro Xaa Xaa Xaa Xaa Xaa Xaa Thr Trp Xaa Xaa Xaa Xaa Xaa Xaa Xaa

20

25

30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa

35

40

<210> 462

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 462

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Gln | Asn | Arg | Tyr | Thr | Asp | Leu | Val | Ala | Ile | Gln | Asn | Lys | Asn | Glu |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

<210> 463

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence:SELECTIN-ANTAGONIST PEPTIDE

<400> 463

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Glu | Asn | Trp | Ala | Asp | Asn | Glu | Pro | Asn | Asn | Lys | Arg | Asn | Asn | Glu |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

Asp

<210> 464

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 464

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Arg | Lys | Asn | Asn | Lys | Thr | Trp | Thr | Trp | Val | Gly | Thr | Lys | Lys | Ala | Leu |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

Thr Asn Glu

<210> 465

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 465

Lys Lys Ala Leu Thr Asn Glu Ala Glu Asn Trp Ala Asp
1 5 10

<210> 466

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 466

Cys Gln Xaa Arg Tyr Thr Asp Leu Val Ala Ile Gln Asn Lys Xaa Glu
1 5 10 15

<210> 467

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 467

Arg Lys Xaa Asn Xaa Xaa Trp Thr Trp Val Gly Thr Xaa Lys Xaa Leu
1 5 10 15

Thr Glu Glu

<210> 468

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 468

Ala Glu Asn Trp Ala Asp Gly Glu Pro Asn Asn Lys Xaa Asn Xaa Glu
1 5 10 15

Asp

<210> 469

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 469

Cys Xaa Xaa Xaa Tyr Thr Xaa Leu Val Ala Ile Gln Asn Lys Xaa Glu
1 5 10 15

<210> 470

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 470

Arg Lys Xaa Xaa Xaa Xaa Trp Xaa Trp Val Gly Thr Xaa Lys Xaa Leu
1 5 10 15

Thr Xaa Glu

<210> 471

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 471

Ala Xaa Asn Trp Xaa Xaa Xaa Glu Pro Asn Asn Xaa Xaa Xaa Glu Asp
1 5 10 15

<210> 472

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SELECTIN
ANTAGONIST PEPTIDE

<400> 472

Xaa Lys Xaa Lys Thr Xaa Glu Ala Xaa Asn Trp Xaa Xaa
1 5 10

<210> 473

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN-MIMETIC PEPTIDE

<220>

<223> At position 1, Xaa is asp-arg-met-pro-cys,
arg-met-pro-cys, met-pro-cys, pro-cys, or cys

<220>

<223> At position 2, Xaa is arg or lys

<220>

<223> At position 10, Xaa is ser or thr

<220>

<223> At position 12, xaa is cys-lys or cys

<400> 473

| | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Xaa | Xaa | Asn | Phe | Phe | Trp | Lys | Thr | Phe | Xaa | Ser | Xaa |
| 1 | | | | 5 | | | | | 10 | | |

<210> 474

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN-MIMETIC PEPTIDE

<400> 474

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asp | Arg | Met | Pro | Cys | Arg | Asn | Phe | Phe | Phe | Trp | Lys | Thr | Phe | Ser | Ser |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

Cys Lys

<210> 475

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN-MIMETIC PEPTIDE

<400> 475

| | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Pro | Cys | Arg | Asn | Phe | Phe | Trp | Lys | Thr | Phe | Ser | Ser | Cys | Lys |
| 1 | | | | 5 | | | | 10 | | | | | 15 | |

<210> 476

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN-MIMETIC PEPTIDE

<400> 476

Cys Arg Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys Lys
1 5 10

<210> 477

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN-MIMETIC PEPTIDE

<400> 477

Asp Arg Met Pro Cys Arg Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys
1 5 10 15

<210> 478

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 478

Met Pro Cys Arg Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys
1 5 10

<210> 479

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/

CORTISTATIN MIMETIC PEPTIDE

<400> 479

Cys Arg Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys
1 5 10

<210> 480

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 480

Asp Arg Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys
1 5 10 15

<210> 481

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 481

Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys Lys
1 5 10 15

<210> 482

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 482

Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys Lys
1 5 10

<210> 483

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 483

Asp Arg Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys
1 5 10 15

<210> 484

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TMP

<400> 484

Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys
1 5 10

<210> 485

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 485

Cys Lys Asn Phe Phe Trp Lys Thr Phe Ser Ser Cys
1 5 10

<210> 486

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 486

Asp Arg Met Pro Cys Arg Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys
1 5 10 15

Lys

<210> 487

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 487

Met Pro Cys Arg Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys Lys
1 5 10 15

<210> 488

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 488

Cys Arg Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys Lys
1 5 10

<210> 489

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 489

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asp | Arg | Met | Pro | Cys | Arg | Asn | Phe | Phe | Trp | Lys | Thr | Phe | Thr | Ser | Cys |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

<210> 490

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 490

| | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Pro | Cys | Arg | Asn | Phe | Phe | Trp | Lys | Thr | Phe | Thr | Ser | Cys |
| 1 | | | | 5 | | | | 10 | | | | | |

<210> 491

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 491

| | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Arg | Asn | Phe | Phe | Trp | Lys | Thr | Phe | Thr | Ser | Cys |
| 1 | | | | 5 | | | | 10 | | | |

<210> 492

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 492

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asp | Arg | Met | Pro | Cys | Lys | Asn | Phe | Phe | Trp | Lys | Thr | Phe | Thr | Ser | Cys |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

Lys

<210> 493

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 493

| | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Pro | Cys | Lys | Asn | Phe | Phe | Trp | Lys | Thr | Phe | Thr | Ser | Cys | Lys |
| 1 | | | | 5 | | | | 10 | | | | | 15 | |

<210> 494

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 494

| | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Lys | Asn | Phe | Phe | Trp | Lys | Thr | Phe | Thr | Ser | Cys | Lys |
| 1 | | | | 5 | | | | 10 | | | | |

<210> 495

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 495

Asp Arg Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys
1 5 10 15

<210> 496

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 496

Met Pro Cys Lys Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys
1 5 10

<210> 497

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:SOMATOSTATIN/
CORTISTATIN MIMETIC PEPTIDE

<400> 497

Cys Lys Asn Phe Phe Trp Lys Thr Phe Thr Ser Cys
1 5 10

<210> 498

<211> 25

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CAP37
MIMETIC/LPS BINDING PEPTIDE

<400> 498

Asn Gln Gly Arg His Phe Cys Gly Gly Ala Leu Ile His Ala Arg Phe
1 5 10 15Val Met Thr Ala Ala Ser Cys Phe Gln
20 25

<210> 499

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CAP37
MIMETIC/LPS BINDING PEPTIDE

<400> 499

Arg His Phe Cys Gly Gly Ala Leu Ile His Ala Arg Phe Val Met Thr
1 5 10 15Ala Ala Ser Cys
20

<210> 500

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CAP37
MIMETIC/LPS BINDING PEPTIDE

<400> 500

Gly Thr Arg Cys Gln Val Ala Gly Trp Gly Ser Gln Arg Ser Gly Gly
1 5 10 15Arg Leu Ser Arg Phe Pro Arg Phe Val Asn Val
20 25

<210> 501
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VEGF-ANTAGONIST
PEPTIDE

<400> 501
Gly Glu Arg Trp Cys Phe Asp Gly Pro Arg Ala Trp Val Cys Gly Trp
1 5 10 15

Glu Ile

<210> 502
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VEGF ANTAGONIST
PEPTIDE

<400> 502
Glu Glu Leu Trp Cys Phe Asp Gly Pro Arg Ala Trp Val Cys Gly Tyr
1 5 10 15

Val Lys

<210> 503
<211> 33
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:ANTIPATHOGENIC
PEPTIDE

<400> 503
Gly Phe Phe Ala Leu Ile Pro Lys Ile Ile Ser Ser Pro Leu Phe Lys

1 5 10 15
Thr Leu Leu Ser Ala Val Gly Ser Ala Leu Ser Ser Ser Gly Gly Gln
20 25 30

Gln

<210> 504

<211> 33

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:ANTIPATHOGENIC
PEPTIDE

<220>

<223> At positions 7, 18 and 19, D amino acid residue

<400> 504

Gly Phe Phe Ala Leu Ile Pro Lys Ile Ile Ser Ser Pro Leu Phe Lys
1 5 10 15

Thr Leu Leu Ser Ala Val Gly Ser Ala Leu Ser Ser Ser Gly Gly Gln
20 25 30

Glu

<210> 505

<211> 22

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:ANTIPATHOGENIC
PEPTIDE

<220>

<223> At positions 18 and 19, D amino acid residues

<400> 505

Gly Phe Phe Ala Leu Ile Pro Lys Ile Ile Ser Ser Pro Leu Phe Lys

1 5 10 15
Thr Leu Leu Ser Ala Val
20

<210> 506
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>
<223> At positions 7, 18 and 19, D amino acid residues

<400> 506
Gly Phe Phe Ala Leu Ile Pro Lys Ile Ile Ser Ser Pro Leu Phe Lys
1 5 10 15
Thr Leu Leu Ser Ala Val
20

<210> 507
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>
<223> At positions 8, 19 and 20, D amino acid residues

<400> 507
Lys Gly Phe Phe Ala Leu Ile Pro Lys Ile Ile Ser Ser Pro Leu Phe
1 5 10 15
Lys Thr Leu Leu Ser Ala Val
20

<210> 508

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At positions 9, 20 and 21, D amino acid residues

<400> 508

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Lys | Gly | Phe | Phe | Ala | Leu | Ile | Pro | Lys | Ile | Ile | Ser | Ser | Pro | Leu |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Lys | Thr | Leu | Leu | Ser | Ala | Val |
| | | | | 20 | | | |

<210> 509

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At positions 9, 20 and 21, D amino acid residues

<400> 509

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Lys | Gly | Phe | Phe | Ala | Leu | Ile | Pro | Lys | Ile | Ile | Ser | Ser | Pro | Leu |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Lys | Thr | Leu | Leu | Ser | Ala | Val |
| | | | | 20 | | | |

<210> 510

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 7, D amino acid residue

<400> 510

Gly Phe Phe Ala Leu Ile Pro Lys Ile Ile Ser
1 5 10

<210> 511

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 511

Gly Ile Gly Ala Val Leu Lys Val Leu Thr Thr Gly Leu Pro Ala Leu
1 5 10 15

Ile Ser Trp Ile Lys Arg Lys Arg Gln Gln
20 25

<210> 512

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At positions 5, 8, 17 and 23, D amino acid
residues

<400> 512

Gly Ile Gly Ala Val Leu Lys Val Leu Thr Thr Gly Leu Pro Ala Leu
1 5 10 15

Ile Ser Trp Ile Lys Arg Lys Arg Gln Gln
20 25

<210> 513

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At positions 5, 8, 17 and 23, D amino acid
residues

<400> 513

Gly Ile Gly Ala Val Leu Lys Val Leu Thr Thr Gly Leu Pro Ala Leu
1 5 10 15

Ile Ser Trp Ile Lys Arg Lys Arg Gln Gln
20 25

<210> 514

<211> 22

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At positions 5, 8, 17 and 21, D amino acid
residues

<400> 514

Gly Ile Gly Ala Val Leu Lys Val Leu Thr Thr Gly Leu Pro Ala Leu
1 5 10 15

Ile Ser Trp Ile Lys Arg
20

<210> 515

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At positions 2, 5, 14 and 18, D amino acid
residues

<400> 515

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Val | Leu | Lys | Val | Leu | Thr | Thr | Gly | Leu | Pro | Ala | Leu | Ile | Ser | Trp |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

Ile Lys Arg

<210> 516

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At positions 3, 4, 8 and 10, D amino acid residues

<400> 516

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Leu | Leu | Leu | Leu | Leu | Lys | Leu | Leu | Leu | Lys |
| 1 | | | | 5 | | | | | 10 | |

<210> 517

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC

PEPTIDE

<220>

<223> At positions 3, 4, 8 and 10, D amino acid residues

<400> 517

Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys

1

5

10

<210> 518

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At positions 3, 4, 8 and 10, D amino acid residues

<400> 518

Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Leu Lys

1

5

10

<210> 519

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 519

Lys Lys Leu Leu Lys Leu Lys Leu Lys Leu Lys Lys

1

5

10

<210> 520

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 520

Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys
1 5 10

<210> 521

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 521

Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Leu Lys
1 5 10

<210> 522

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 522

Lys Leu Leu Leu Lys
1 5

<210> 523

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC

PEPTIDE

<400> 523

Lys Leu Leu Leu Lys Leu Leu Lys
1 5

<210> 524

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 524

Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Leu Lys
1 5 10

<210> 525

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 525

Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Leu Lys
1 5 10

<210> 526

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 526

Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Leu Lys
1 5 10

<210> 527

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 527

Lys Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Lys
1 5 10

<210> 528

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 528

Lys Val Val Val Lys Val Val Val Lys Val Val Lys
1 5 10

<210> 529

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 529

Lys Val Val Val Lys Val Lys Val Lys Val Val Lys
1 5 10

<210> 530
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 530
Lys Val Val Val Lys Val Lys Val Lys Val Lys
1 5 10

<210> 531
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 531
Lys Val Val Val Lys Val Lys Val Lys Val Val Lys
1 5 10

<210> 532
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 532
Lys Leu Ile Leu Lys Leu
1 5

<210> 533

<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 533
Lys Val Leu His Leu Leu
1 5

<210> 534
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 534
Leu Lys Leu Arg Leu Leu
1 5

<210> 535
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 535
Lys Pro Leu His Leu Leu
1 5

<210> 536
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 536

Lys Leu Ile Leu Lys Leu Val Arg
1 5

<210> 537

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 537

Lys Val Phe His Leu Leu His Leu
1 5

<210> 538

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 538

His Lys Phe Arg Ile Leu Lys Leu
1 5

<210> 539

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC

PEPTIDE

<400> 539

Lys Pro Phe His Ile Leu His Leu
1 5

<210> 540

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 540

Lys Ile Ile Ile Lys Ile Lys Ile Lys Ile Ile Lys
1 5 10

<210> 541

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 541

Lys Ile Ile Ile Lys Ile Lys Ile Lys Ile Ile Lys
1 5 10

<210> 542

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 542

Lys Ile Ile Ile Lys Ile Lys Ile Lys Ile Ile Lys
1 5 10

<210> 543

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 543

Lys Ile Pro Ile Lys Ile Lys Ile Lys Ile Pro Lys
1 5 10

<210> 544

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 544

Lys Ile Pro Ile Lys Ile Lys Ile Lys Ile Val Lys
1 5 10

<210> 545

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 545

Arg Ile Ile Ile Arg Ile Arg Ile Arg Ile Ile Arg
1 5 10

<210> 546
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 546
Arg Ile Ile Ile Arg Ile Arg Ile Arg Ile Ile Arg
1 5 10

<210> 547
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 547
Arg Ile Ile Ile Arg Ile Arg Ile Arg Ile Ile Arg
1 5 10

<210> 548
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 548
Arg Ile Val Ile Arg Ile Arg Ile Arg Leu Ile Arg
1 5 10

<210> 549

<211> 12
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 549

Arg Ile Ile Val Arg Ile Arg Leu Arg Ile Ile Arg
1 5 10

<210> 550

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 550

Arg Ile Gly Ile Arg Leu Arg Val Arg Ile Ile Arg
1 5 10

<210> 551

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 551

Lys Ile Val Ile Arg Ile Arg Ile Arg Leu Ile Arg
1 5 10

<210> 552

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 552

Arg Ile Ala Val Lys Trp Arg Leu Arg Phe Ile Lys
1 5 10

<210> 553

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 553

Lys Ile Gly Trp Lys Leu Arg Val Arg Ile Ile Arg
1 5 10

<210> 554

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 554

Lys Lys Ile Gly Trp Leu Ile Ile Arg Val Arg Arg
1 5 10

<210> 555

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC

PEPTIDE

<400> 555

Arg Ile Val Ile Arg Ile Arg Ile Arg Leu Ile Arg Ile Arg
1 5 10

<210> 556

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 556

Arg Ile Ile Val Arg Ile Arg Leu Arg Ile Ile Arg Val Arg
1 5 10

<210> 557

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 557

Arg Ile Gly Ile Arg Leu Arg Val Arg Ile Ile Arg Arg Val
1 5 10

<210> 558

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 558

Lys Ile Val Ile Arg Ile Arg Ala Arg Leu Ile Arg Ile Arg Ile Arg
1 5 10 15

<210> 559

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 559

Arg Ile Ile Val Lys Ile Arg Leu Arg Ile Ile Lys Lys Ile Arg Leu
1 5 10 15

<210> 560

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 560

Lys Ile Gly Ile Lys Ala Arg Val Arg Ile Ile Arg Val Lys Ile Ile
1 5 10 15

<210> 561

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 561

Arg Ile Ile Val His Ile Arg Leu Arg Ile Ile His His Ile Arg Leu
1 5 10 15

<210> 562
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 562
His Ile Gly Ile Lys Ala His Val Arg Ile Ile Arg Val His Ile Ile
1 5 10 15

<210> 563
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 563
Arg Ile Tyr Val Lys Ile His Leu Arg Tyr Ile Lys Lys Ile Arg Leu
1 5 10 15

<210> 564
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 564
Lys Ile Gly His Lys Ala Arg Val His Ile Ile Arg Tyr Lys Ile Ile
1 5 10 15

<210> 565

<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 565
Arg Ile Tyr Val Lys Pro His Pro Arg Tyr Ile Lys Lys Ile Arg Leu
1 5 10 15

<210> 566
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 566
Lys Pro Gly His Lys Ala Arg Pro His Ile Ile Arg Tyr Lys Ile Ile
1 5 10 15

<210> 567
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 567
Lys Ile Val Ile Arg Ile Arg Ile Arg Leu Ile Arg Ile Arg Ile Arg
1 5 10 15

Lys Ile Val

<210> 568

<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 568
Arg Ile Ile Val Lys Ile Arg Leu Arg Ile Ile Lys Lys Ile Arg Leu
1 5 10 15

Ile Lys Lys

<210> 569
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 569
Lys Ile Gly Trp Lys Leu Arg Val Arg Ile Ile Arg Val Lys Ile Gly
1 5 10 15

Arg Leu Arg

<210> 570
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 570
Lys Ile Val Ile Arg Ile Arg Ile Arg Leu Ile Arg Ile Arg Ile Arg
1 5 10 15

Lys Ile Val Lys Val Lys Arg Ile Arg
20 25

<210> 571

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 571

Arg Phe Ala Val Lys Ile Arg Leu Arg Ile Ile Lys Lys Ile Arg Leu
1 5 10 15

Ile Lys Lys Ile Arg Lys Arg Val Ile Lys
20 25

<210> 572

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 572

Lys Ala Gly Trp Lys Leu Arg Val Arg Ile Ile Arg Val Lys Ile Gly
1 5 10 15

Arg Leu Arg Lys Ile Gly Trp Lys Lys Arg Val Arg Ile Lys
20 25 30

<210> 573

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC

PEPTIDE

<400> 573

Arg Ile Tyr Val Lys Pro His Pro Arg Tyr Ile Lys Lys Ile Arg Leu
1 5 10 15

<210> 574

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 574

Lys Pro Gly His Lys Ala Arg Pro His Ile Ile Arg Tyr Lys Ile Ile
1 5 10 15

<210> 575

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 575

Lys Ile Val Ile Arg Ile Arg Ile Arg Leu Ile Arg Ile Arg Ile Arg
1 5 10 15

Lys Ile Val

<210> 576

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC

PEPTIDE

<400> 576

Arg Ile Ile Val Lys Ile Arg Leu Arg Ile Ile Lys Lys Ile Arg Leu
1 5 10 15

Ile Lys Lys

<210> 577

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 577

Arg Ile Tyr Val Ser Lys Ile Ser Ile Tyr Ile Lys Lys Ile Arg Leu
1 5 10 15

<210> 578

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 578

Lys Ile Val Ile Phe Thr Arg Ile Arg Leu Thr Ser Ile Arg Ile Arg
1 5 10 15

Ser Ile Val

<210> 579

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 579

Lys Pro Ile His Lys Ala Arg Pro Thr Ile Ile Arg Tyr Lys Met Ile
1 5 10 15

<210> 580

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 1, disulfide bond to position 26

<220>

<223> At position 26, disulfide bond to position 1

<400> 580

Xaa Cys Lys Gly Phe Phe Ala Leu Ile Pro Lys Ile Ile Ser Ser Pro
1 5 10 15Leu Phe Lys Thr Leu Leu Ser Ala Val Cys
20 25

<210> 581

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 581

Cys Lys Lys Gly Phe Phe Ala Leu Ile Pro Lys Ile Ile Ser Ser Pro
1 5 10 15

Leu Phe Lys Thr Leu Leu Ser Ala Val Cys
20 25

<210> 582
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 582
Cys Lys Lys Lys Gly Phe Phe Ala Leu Ile Pro Lys Ile Ile Ser Ser
1 5 10 15

Pro Leu Phe Lys Thr Leu Leu Ser Ala Val Cys
20 25

<210> 583
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>
<223> At position 1, disulfide bond to position 17

<220>
<223> At position 17, disulfide bond to position 1

<400> 583
Xaa Cys Arg Ile Val Ile Arg Ile Arg Ile Arg Leu Ile Arg Ile Arg
1 5 10 15

Cys

<210> 584

<211> 19
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 1, disulfide bond to position 19

<220>

<223> At position 19, disulfide bond to position 1

<400> 584

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Xaa | Cys | Lys | Pro | Gly | His | Lys | Ala | Arg | Pro | His | Ile | Ile | Arg | Tyr | Lys |
| 1 | | | | | 5 | | | | 10 | | | | | 15 | |

Ile Ile Cys

<210> 585

<211> 29

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 1, disulfide bond to position 29

<220>

<223> At position 29, disulfide bond to position 1

<400> 585

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Xaa | Cys | Arg | Phe | Ala | Val | Lys | Ile | Arg | Leu | Arg | Ile | Ile | Lys | Lys | Ile |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

| | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Arg | Leu | Ile | Lys | Lys | Ile | Arg | Lys | Arg | Val | Ile | Lys | Cys |
| | | | 20 | | | | | 25 | | | | |

<210> 586

<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 586
Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys Cys
1 5 10

<210> 587
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 587
Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys
1 5 10

<210> 588
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 588
Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Leu Lys Cys
1 5 10

<210> 589
<211> 12
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 589

Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys
1 5 10

<210> 590

<211> 28

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 590

His Ser Asp Ala Val Phe Tyr Asp Asn Tyr Thr Arg Leu Arg Lys Gln
1 5 10 15Met Ala Val Lys Lys Tyr Leu Asn Ser Ile Leu Asn
20 25

<210> 591

<211> 31

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 591

Asn Leu Glu His Ser Asp Ala Val Phe Tyr Asp Asn Tyr Thr Arg Leu
1 5 10 15Arg Lys Gln Met Ala Val Lys Lys Tyr Leu Asn Ser Ile Leu Asn
20 25 30

<210> 592

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 1, Xaa is absent or is ala, val,
ala-val, val-ala, L-lys, D-lys, ala-lys, val-lys,
ala-val-lys, val-ala-lys, or an ornithinyl residue

<220>

<223> At position 2, Xaa is L-lys, D-lys or an
ornithinyl residue

<220>

<223> At position 3, Xaa is L-tyr, D-tyr, phe, trp or a
p-aminophenylalanyl residue

<220>

<223> At position 4, Xaa is a hydrophobic aliphatic
amino acid residue (X5), X5-leu, X5-norleucyl,
X5-D-ala, X5-asn-ser, X5-asn-ser-ile,
X5-asn-ser-tyr, X5-asn-ser-ile-leu,
X5-asn-ser-tyr-leu,

<220>

<223> or X5-asn-ser-tyr-leu-asn

<400> 592

Xaa Xaa Xaa Xaa

1

<210> 593

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 1, Xaa is either absent, a hydrophobic

aliphatic residue (X5), X5-asn, tyr-X5, lys-X5,
 lyx-S5-asn, lys-tyr-X5, lys-tyr-X5-as,
 lys-lys-tyr-X5, lys-lys-tyr-X5-asn,
 val-lys-lys-tyr-X5,

<220>

<223> val-ala-lys-lys-tyr-X5-asn, or
 ala-val-lys-lys-tyr-X5-asn

<220>

<223> At position 3, Xaa is ile or tyr

<400> 593

Xaa Ser Xaa Leu Asn

1

5

<210> 594

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
 PEPTIDE

<220>

<223> At positions 1 and 6, Xaa are cross-linked amino
 acid residues in which the sidechain linker group
 is (CH₂)_m-Z-(CH₂)_n wherein Z is -CONH-, -NHCO-,
 -S-S-, -S(CH₂)tCO-NH or -NH-CO(CH₂)tS-; m is 1 or
 2

<220>

<223> when Z is -NH-CO- or -NH-CO(CH₂)tS-; n is 1 or 2
 when Z is -NH-CO-, -S-S- or -NH-CO(CH₂)tS, or n is
 2, 3 or 4 when Z is -CONH- or -S(CH₂)tCO-NH-

<220>

<223> At position 5, Xaa is a hydrophobic aliphatic
 amino acid residue

<220>

<223> At position 7, Xaa is a covalent bond or Asn, Ser,
 Ile, Tyr, Leu, Asn-Ser, Asn-Ser-Ile, Asn-Ser-Tyr,
 Asn-Ser-Ile-Leu, Asn-Ser-Tyr-Leu,
 Asn-Ser-Ile-Leu-Asn or Asn-Ser-Tyr-Leu-Asn

<400> 594

Xaa Lys Lys Tyr Xaa Xaa Xaa

1

5

<210> 595

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 595

Lys Lys Tyr Leu

1

<210> 596

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 596

Asn Ser Ile Leu Asn

1

5

<210> 597

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 597

Lys Lys Tyr Leu

1

<210> 598

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 4, D amino acid residue

<400> 598

Lys Lys Tyr Ala

1

<210> 599

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 599

Ala Val Lys Lys Tyr Leu

1

5

<210> 600

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 600

Asn Ser Ile Leu Asn

1

5

<210> 601

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 601

Lys Lys Tyr Val

1

<210> 602

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 3, Xaa is a lauric acid residue

<400> 602

Ser Ile Xaa Asn

1

<210> 603

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 5, Xaa is a norleucyl residue

<400> 603

Lys Lys Tyr Leu Xaa
1 5

<210> 604

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 604

Asn Ser Tyr Leu Asn
1 5

<210> 605

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 605

Asn Ser Ile Tyr Asn
1 5

<210> 606

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 606

Lys Lys Tyr Leu Pro Pro Asn Ser Ile Leu Asn

1

5

10

<210> 607

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 1, Xaa is a lauric acid residue

<400> 607

Xaa Lys Lys Tyr Leu

1

5

<210> 608

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 1, Xaa is a caproic acid residue

<400> 608

Xaa Lys Lys Tyr Leu

1

5

<210> 609

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 4, Xaa is a norleucyl residue

<400> 609

Lys Lys Tyr Xaa

1

<210> 610

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 610

Val Lys Lys Tyr Leu

1

5

<210> 611

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 611

Leu Asn Ser Ile Leu Asn

1

5

<210> 612

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 612

Tyr Leu Asn Ser Ile Leu Asn
1 5

<210> 613

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 613

Lys Lys Tyr Leu Asn
1 5

<210> 614

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 614

Lys Lys Tyr Leu Asn Ser
1 5

<210> 615

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 615

Lys Lys Tyr Leu Asn Ser Ile

1

5

<210> 616

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 616

Lys Lys Tyr Leu Asn Ser Ile Leu

1

5

<210> 617

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 617

Lys Lys Tyr Leu

1

<210> 618

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 618

Lys Lys Tyr Asp Ala

1

5

<210> 619
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 619
Ala Val Lys Lys Tyr Leu
1 5

<210> 620
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 620
Asn Ser Ile Leu Asn
1 5

<210> 621
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 621
Lys Lys Tyr Val
1

<210> 622
<211> 4

<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>
<223> At position 3, Xaa is a lauric acid residue

<400> 622
Ser Ile Xaa Asn
1

<210> 623
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 623
Asn Ser Tyr Leu Asn
1 5

<210> 624
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 624
Asn Ser Ile Tyr Asn
1 5

<210> 625
<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 5, Xaa is a norleucyl residue

<400> 625

Lys Lys Tyr Leu Xaa
1 5

<210> 626

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 626

Lys Lys Tyr Leu Pro Pro Asn Ser Ile Leu Asn
1 5 10

<210> 627

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 627

Lys Lys Tyr Leu
1

<210> 628

<211> 5

<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 628

Lys Lys Tyr Asp Ala
1 5

<210> 629

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 629

Ala Val Lys Lys Tyr Leu
1 5

<210> 630

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 630

Asn Ser Ile Leu Asn
1 5

<210> 631

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 631

Lys Lys Tyr Val

1

<210> 632

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 3, Xaa is a lauric acid residue

<400> 632

Ser Ile Xaa Asn

1

<210> 633

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 633

Leu Ala Lys Lys Tyr Leu

1

5

<210> 634

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 634

Cys Ala Pro Lys Lys Tyr Leu
1 5

<210> 635

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 4, Xaa is a norleucyl residue

<400> 635

Lys Lys Tyr Xaa
1

<210> 636

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 636

Val Lys Lys Tyr Leu
1 5

<210> 637

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 637

Leu Asn Ser Ile Leu Asn
1 5

<210> 638

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 638

Tyr Leu Asn Ser Ile Leu Asn
1 5

<210> 639

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 5, Xaa is a norleucyl residue

<400> 639

Lys Lys Tyr Leu Xaa
1 5

<210> 640

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 640

Lys Lys Tyr Leu Asn
1 5

<210> 641

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 641

Lys Lys Tyr Leu Asn Ser
1 5

<210> 642

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 642

Lys Lys Tyr Leu Asn Ser Ile
1 5

<210> 643

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 643

Lys Lys Tyr Leu Asn Ser Ile Leu

1

5

<210> 644

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 644

Lys Lys Lys Tyr Leu Asp

1

5

<210> 645

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At positions 1, 6 disulfide cross-linked

<400> 645

Xaa Cys Lys Lys Tyr Leu Cys

1

5

<210> 646

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At positions 1, 6 cross-linked by S-CH₂-CO

<400> 646

Cys Lys Lys Tyr Leu Lys

1

5

<210> 647

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<220>

<223> At position 4, D amino acid residue

<400> 647

Lys Lys Tyr Ala

1

<210> 648

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 648

Trp Trp Thr Asp Thr Gly Leu Trp

1

5

<210> 649

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 649

Trp Trp Thr Asp Asp Gly Leu Trp
1 5

<210> 650

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 650

Trp Trp Asp Thr Arg Gly Leu Trp Val Trp Thr Ile
1 5 10

<210> 651

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 651

Phe Trp Gly Asn Asp Gly Ile Trp Leu Glu Ser Gly
1 5 10

<210> 652

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 652

Asp Trp Asp Gln Phe Gly Leu Trp Arg Gly Ala Ala
1 5 10

<210> 653

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 653

Arg Trp Asp Asp Asn Gly Leu Trp Val Val Val Leu
1 5 10

<210> 654

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 654

Ser Gly Met Trp Ser His Tyr Gly Ile Trp Met Gly
1 5 10

<210> 655

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 655

Gly Gly Arg Trp Asp Gln Ala Gly Leu Trp Val Ala

1 5 10

<210> 656

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 656

Lys Leu Trp Ser Glu Gln Gly Ile Trp Met Gly Glu

1 5 10

<210> 657

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 657

Cys Trp Ser Met His Gly Leu Trp Leu Cys

1 5 10

<210> 658

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 658

Gly Cys Trp Asp Asn Thr Gly Ile Trp Val Pro Cys

1 5 10

<210> 659
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 659
Asp Trp Asp Thr Arg Gly Leu Trp Val Tyr
1 5 10

<210> 660
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 660
Ser Leu Trp Asp Glu Asn Gly Ala Trp Ile
1 5 10

<210> 661
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 661
Lys Trp Asp Asp Arg Gly Leu Trp Met His
1 5 10

<210> 662
<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 662

Gln Ala Trp Asn Glu Arg Gly Leu Trp Thr
1 5 10

<210> 663

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 663

Gln Trp Asp Thr Arg Gly Leu Trp Val Ala
1 5 10

<210> 664

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 664

Trp Asn Val His Gly Ile Trp Gln Glu
1 5

<210> 665

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 665

Ser Trp Asp Thr Arg Gly Leu Trp Val Glu
1 5 10

<210> 666

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 666

Asp Trp Asp Thr Arg Gly Leu Trp Val Ala
1 5 10

<210> 667

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 667

Ser Trp Gly Arg Asp Gly Leu Trp Ile Glu
1 5 10

<210> 668

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 668

Glu Trp Thr Asp Asn Gly Leu Trp Ala Leu

1 5 10

<210> 669

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 669

Ser Trp Asp Glu Lys Gly Leu Trp Ser Ala

1 5 10

<210> 670

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VIP MIMETIC
PEPTIDE

<400> 670

Ser Trp Asp Ser Ser Gly Leu Trp Met Asp

1 5 10

<210> 671

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 671

Ser His Leu Tyr Trp Gln Pro Tyr Ser Val Gln

1 5 10

<210> 672

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 672

Thr Leu Val Tyr Trp Gln Pro Tyr Ser Leu Gln Thr
1 5 10

<210> 673

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 673

Arg Gly Asp Tyr Trp Gln Pro Tyr Ser Val Gln Ser
1 5 10

<210> 674

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 674

Val His Val Tyr Trp Gln Pro Tyr Ser Val Gln Thr
1 5 10

<210> 675
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 675
Arg Leu Val Tyr Trp Gln Pro Tyr Ser Val Gln Thr
1 5 10

<210> 676
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 676
Ser Arg Val Tyr Phe Gln Pro Tyr Ser Leu Gln Ser
1 5 10

<210> 677
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 677
Asn Met Val Tyr Trp Gln Pro Tyr Ser Ile Gln Thr
1 5 10

<210> 678
<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 678

Ser Val Val Phe Trp Gln Pro Tyr Ser Val Gln Thr
1 5 10

<210> 679

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 679

Thr Phe Val Tyr Trp Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 680

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 680

Thr Leu Val Tyr Trp Gln Pro Tyr Ser Ile Gln Arg
1 5 10

<210> 681

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 681

Arg Leu Val Tyr Trp Gln Pro Tyr Ser Val Gln Arg
1 5 10

<210> 682

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 682

Ser Pro Val Phe Trp Gln Pro Tyr Ser Ile Gln Ile
1 5 10

<210> 683

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 683

Trp Ile Glu Trp Trp Gln Pro Tyr Ser Val Gln Ser
1 5 10

<210> 684

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 684

Ser Leu Ile Tyr Trp Gln Pro Tyr Ser Leu Gln Met
1 5 10

<210> 685

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 685

Thr Arg Leu Tyr Trp Gln Pro Tyr Ser Val Gln Arg
1 5 10

<210> 686

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 686

Arg Cys Asp Tyr Trp Gln Pro Tyr Ser Val Gln Thr
1 5 10

<210> 687

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 687

Met Arg Val Phe Trp Gln Pro Tyr Ser Val Gln Asn

1 5 10

<210> 688

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 688

Lys Ile Val Tyr Trp Gln Pro Tyr Ser Val Gln Thr

1 5 10

<210> 689

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 689

Arg His Leu Tyr Trp Gln Pro Tyr Ser Val Gln Arg

1 5 10

<210> 690

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 690

Ala Leu Val Trp Trp Gln Pro Tyr Ser Glu Gln Ile

1 5 10

<210> 691
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 691
Ser Arg Val Trp Phe Gln Pro Tyr Ser Leu Gln Ser
1 5 10

<210> 692
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 692
Trp Glu Gln Pro Tyr Ala Leu Pro Leu Glu
1 5 10

<210> 693
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 693
Gln Leu Val Trp Trp Gln Pro Tyr Ser Val Gln Arg
1 5 10

<210> 694
<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 694

Asp Leu Arg Tyr Trp Gln Pro Tyr Ser Val Gln Val
1 5 10

<210> 695

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 695

Glu Leu Val Trp Trp Gln Pro Tyr Ser Leu Gln Leu
1 5 10

<210> 696

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 696

Asp Leu Val Trp Trp Gln Pro Tyr Ser Val Gln Trp
1 5 10

<210> 697

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

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Asn Gly Asn Tyr Trp Gln Pro Tyr Ser Phe Gln Val
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<210> 698

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
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<400> 698

Glu Leu Val Tyr Trp Gln Pro Tyr Ser Ile Gln Arg
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Glu Leu Met Tyr Trp Gln Pro Tyr Ser Val Gln Glu
1 5 10

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Asn Leu Leu Tyr Trp Gln Pro Tyr Ser Met Gln Asp
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Gly Tyr Glu Trp Tyr Gln Pro Tyr Ser Val Gln Arg
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Ser Arg Val Trp Tyr Gln Pro Tyr Ser Val Gln Arg
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Leu Ser Glu Gln Tyr Gln Pro Tyr Ser Val Gln Arg

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<400> 705

Val Gly Arg Trp Tyr Gln Pro Tyr Ser Val Gln Arg
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PEPTIDE

<400> 706

Val His Val Tyr Trp Gln Pro Tyr Ser Val Gln Arg
1 5 10

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PEPTIDE

<400> 707
Gln Ala Arg Trp Tyr Gln Pro Tyr Ser Val Gln Arg
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<210> 708
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PEPTIDE

<400> 708
Val His Val Tyr Trp Gln Pro Tyr Ser Val Gln Thr
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Arg Ser Val Tyr Trp Gln Pro Tyr Ser Val Gln Arg
1 5 10

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Thr Arg Val Trp Phe Gln Pro Tyr Ser Val Gln Arg
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<400> 711

Gly Arg Ile Trp Phe Gln Pro Tyr Ser Val Gln Arg
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Gly Arg Val Trp Phe Gln Pro Tyr Ser Val Gln Arg
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Ala Arg Thr Trp Tyr Gln Pro Tyr Ser Val Gln Arg
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Ala Arg Val Trp Trp Gln Pro Tyr Ser Val Gln Met
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<400> 715

Arg Leu Met Phe Tyr Gln Pro Tyr Ser Val Gln Arg
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Glu Ser Met Trp Tyr Gln Pro Tyr Ser Val Gln Arg
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His Phe Gly Trp Trp Gln Pro Tyr Ser Val His Met
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Ala Arg Phe Trp Trp Gln Pro Tyr Ser Val Gln Arg
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Arg Leu Val Tyr Trp Gln Pro Tyr Ala Pro Ile Tyr

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Arg Leu Val Tyr Trp Gln Pro Tyr Ser Val Gln Ala

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Ser Arg Val Trp Tyr Gln Pro Tyr Ala Lys Gly Leu
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Ser Arg Val Trp Tyr Gln Pro Tyr Ala Gln Gly Leu
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Ser Arg Val Trp Tyr Gln Pro Tyr Ala Met Pro Leu
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Ser Arg Val Trp Tyr Gln Pro Tyr Ser Val Gln Ala
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<400> 727

Ser Arg Val Trp Tyr Gln Pro Tyr Ser Leu Gly Leu
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Ser Arg Val Trp Tyr Gln Pro Tyr Ala Arg Glu Leu
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Ser Arg Ile Trp Trp Gln Pro Tyr Ala Leu Pro Leu
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<210> 734

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Asp Pro Leu Phe Trp Gln Pro Tyr Ala Leu Pro Leu
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<210> 735

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<400> 735

Ser Arg Gln Trp Val Gln Pro Tyr Ala Leu Pro Leu

1 5 10

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Ile Arg Ser Trp Trp Gln Pro Tyr Ala Leu Pro Leu
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PEPTIDE

<400> 737

Arg Gly Tyr Trp Gln Pro Tyr Ala Leu Pro Leu
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Arg Leu Leu Trp Val Gln Pro Tyr Ala Leu Pro Leu
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Glu Tyr Arg Trp Phe Gln Pro Tyr Ala Leu Pro Leu
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Asp Ser Ser Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
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Ile Gly Asn Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
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Asn Leu Arg Trp Asp Gln Pro Tyr Ala Leu Pro Leu
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<400> 747

Leu Pro Glu Phe Trp Gln Pro Tyr Ala Leu Pro Leu
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<210> 748

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<400> 748

Asp Ser Tyr Trp Trp Gln Pro Tyr Ala Leu Pro Leu
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<210> 749

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<400> 749

Arg Ser Gln Tyr Tyr Gln Pro Tyr Ala Leu Pro Leu
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Ala Arg Phe Trp Leu Gln Pro Tyr Ala Leu Pro Leu
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<210> 751

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<400> 751

Asn Ser Tyr Phe Trp Gln Pro Tyr Ala Leu Pro Leu

1 5 10

<210> 752
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PEPTIDE

<400> 752
Arg Phe Met Tyr Trp Gln Pro Tyr Ser Val Gln Arg
1 5 10

<210> 753
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<400> 753
Ala His Leu Phe Trp Gln Pro Tyr Ser Val Gln Arg
1 5 10

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<400> 754
Trp Trp Gln Pro Tyr Ala Leu Pro Leu
1 5

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Tyr Tyr Gln Pro Tyr Ala Leu Pro Leu
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<400> 756

Tyr Phe Gln Pro Tyr Ala Leu Gly Leu
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Tyr Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
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<400> 758

Arg Trp Trp Gln Pro Tyr Ala Thr Pro Leu
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Gly Trp Tyr Gln Pro Tyr Ala Leu Gly Phe
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<400> 760

Tyr Trp Tyr Gln Pro Tyr Ala Leu Gly Leu
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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 761

Ile Trp Tyr Gln Pro Tyr Ala Met Pro Leu
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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
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<400> 762

Ser Asn Met Gln Pro Tyr Gln Arg Leu Ser
1 5 10

<210> 763

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PEPTIDE

<400> 763

Thr Phe Val Tyr Trp Gln Pro Tyr Ala Val Gly Leu Pro Ala Ala Glu
1 5 10 15Thr Ala Cys Asn
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<210> 764

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Thr Phe Val Tyr Trp Gln Pro Tyr Ser Val Gln Met Thr Ile Thr Gly
1 5 10 15Lys Val Thr Met
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<210> 765

<211> 20

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<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
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Thr Phe Val Tyr Trp Gln Pro Tyr Ser Ser His Xaa Xaa Val Pro Xaa
1 5 10 15Gly Phe Pro Leu
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<210> 766

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<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
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<400> 766

Thr Phe Val Tyr Trp Gln Pro Tyr Tyr Gly Asn Pro Gln Trp Ala Ile
1 5 10 15His Val Arg His
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<210> 767
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<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 767

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| Thr | Phe | Val | Tyr | Trp | Gln | Pro | Tyr | Val | Leu | Leu | Glu | Leu | Pro | Glu | Gly |
| 1 | | | | 5 | | | | 10 | | | | | 15 | | |

Ala Val Arg Ala
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PEPTIDE

<400> 768

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| Thr | Phe | Val | Tyr | Trp | Gln | Pro | Tyr | Val | Asp | Tyr | Val | Trp | Pro | Ile | Pro |
| 1 | | | | 5 | | | | 10 | | | | | 15 | | |

Ile Ala Gln Val
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Gly Trp Tyr Gln Pro Tyr Val Asp Gly Trp Arg

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<400> 770

Arg Trp Glu Gln Pro Tyr Val Lys Asp Gly Trp Ser
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<400> 771

Glu Trp Tyr Gln Pro Tyr Ala Leu Gly Trp Ala Arg
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<400> 772

Gly Trp Trp Gln Pro Tyr Ala Arg Gly Leu
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<400> 773

Leu Phe Glu Gln Pro Tyr Ala Lys Ala Leu Gly Leu
1 5 10

<210> 774

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<400> 774

Gly Trp Glu Gln Pro Tyr Ala Arg Gly Leu Ala Gly
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<210> 775

<211> 12

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
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<400> 775

Ala Trp Val Gln Pro Tyr Ala Thr Pro Leu Asp Glu
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<210> 776

<211> 12

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 776

Met Trp Tyr Gln Pro Tyr Ser Ser Gln Pro Ala Glu
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<210> 777

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 777

Gly Trp Thr Gln Pro Tyr Ser Gln Gln Gly Glu Val
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<210> 778

<211> 12

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
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<400> 778

Asp Trp Phe Gln Pro Tyr Ser Ile Gln Ser Asp Glu
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<210> 779

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<400> 779

Pro Trp Ile Gln Pro Tyr Ala Arg Gly Phe Gly
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<210> 780

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Arg Pro Leu Tyr Trp Gln Pro Tyr Ser Val Gln Val
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<210> 781

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<400> 781

Thr Leu Ile Tyr Trp Gln Pro Tyr Ser Val Gln Ile
1 5 10

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<400> 782

Arg Phe Asp Tyr Trp Gln Pro Tyr Ser Asp Gln Thr
1 5 10

<210> 783

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<400> 783

Trp His Gln Phe Val Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 784

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<400> 784

Glu Trp Asp Ser Val Tyr Trp Gln Pro Tyr Ser Val Gln Thr Leu Leu
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Arg

<210> 785

<211> 17

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<400> 785

Trp Glu Gln Asn Val Tyr Trp Gln Pro Tyr Ser Val Gln Ser Phe Ala
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Asp

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PEPTIDE

<400> 786

Ser Asp Val Val Tyr Trp Gln Pro Tyr Ser Val Gln Ser Leu Glu Met
1 5 10 15

<210> 787

<211> 17

<212> PRT

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<400> 787

Tyr Tyr Asp Gly Val Tyr Trp Gln Pro Tyr Ser Val Gln Val Met Pro
1 5 10 15

Ala

<210> 788

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PEPTIDE

<400> 788

Ser Asp Ile Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 789

Gln Arg Ile Trp Trp Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 790

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 790

Ser Arg Ile Trp Trp Gln Pro Tyr Ala Leu Pro Leu
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<210> 791

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 791

Arg Ser Leu Tyr Trp Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 792

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 792

Thr Ile Ile Trp Glu Gln Pro Tyr Ala Leu Pro Leu
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<210> 793

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 793

Trp Glu Thr Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 794

<211> 12

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 794

Ser Tyr Asp Trp Glu Gln Pro Tyr Ala Leu Pro Leu

1 5 10

<210> 795

<211> 12

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 795

Ser Arg Ile Trp Cys Gln Pro Tyr Ala Leu Pro Leu

1 5 10

<210> 796

<211> 12

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 796

Glu Ile Met Phe Trp Gln Pro Tyr Ala Leu Pro Leu

1 5 10

<210> 797

<211> 12

<212> PRT

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 797

Asp Tyr Val Trp Gln Gln Pro Tyr Ala Leu Pro Leu

1 5 10

<210> 798

<211> 15

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 798

Met Asp Leu Leu Val Gln Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 799

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<212> PRT

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 799

Gly Ser Lys Val Ile Leu Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 800

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<212> PRT

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 800

Arg Gln Gly Ala Asn Ile Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 801

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<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 801

Gly Gly Gly Asp Glu Pro Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 802

<211> 15

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 802

Ser Gln Leu Glu Arg Thr Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 803

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 803

Glu Thr Trp Val Arg Glu Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 804

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 804

Lys Lys Gly Ser Thr Gln Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 805

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 805

Leu Gln Ala Arg Met Asn Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 806

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
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<400> 806

Glu Pro Arg Ser Gln Lys Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 807

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 807

Val Lys Gln Lys Trp Arg Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 808

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 808

Leu Arg Arg His Asp Val Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 809

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 809

Arg Ser Thr Ala Ser Ile Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 810

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<212> PRT

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 810

Glu Ser Lys Glu Asp Gln Trp Tyr Gln Pro Tyr Ala Leu Pro Leu

1 5 10 15

<210> 811

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<212> PRT

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
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<400> 811

Glu Gly Ser Arg Glu Gly Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 812

<211> 15

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
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<400> 812

Glu Gly Ser Arg Glu Gly Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 813

<211> 12

<212> PRT

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 813

Val Ile Glu Trp Trp Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 814

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 814

Val Trp Tyr Trp Glu Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 815

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 815

Ala Ser Glu Trp Trp Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 816

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 816

Phe Tyr Glu Trp Trp Gln Pro Tyr Ala Leu Pro Leu
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<210> 817

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 817

Glu Gly Trp Trp Val Gln Pro Tyr Ala Leu Pro Leu
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<210> 818

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<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
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<400> 818

Trp Gly Glu Trp Leu Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 819

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 819

Asp Tyr Val Trp Glu Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 820

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 820

Ala His Thr Trp Trp Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 821

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 821

Phe Ile Glu Trp Phe Gln Pro Tyr Ala Leu Pro Leu
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<210> 822

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 822

Trp Leu Ala Trp Glu Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 823

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 823

Val Met Glu Trp Trp Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 824

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<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 824

Glu Arg Met Trp Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 825

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<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 825

Asn Xaa Xaa Trp Xaa Xaa Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 826

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 826

Trp Gly Asn Trp Tyr Gln Pro Tyr Ala Leu Pro Leu

1 5 10

<210> 827

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 827

Thr Leu Tyr Trp Glu Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 828

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 828

Val Trp Arg Trp Glu Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 829

<211> 11

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 829

Leu Leu Trp Thr Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 830
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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 830

Ser Arg Ile Trp Xaa Xaa Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 831

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<212> PRT

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 831

Ser Asp Ile Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 832

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 832

Trp Gly Tyr Tyr Xaa Xaa Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 833

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 833

Thr Ser Gly Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 834

<211> 12

<212> PRT

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 834

Val His Pro Tyr Xaa Xaa Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 835

<211> 12

<212> PRT

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 835

Glu His Ser Tyr Phe Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 836

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 836

Xaa Xaa Ile Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 837

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 837

Ala Gln Leu His Ser Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 838

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 838

Trp Ala Asn Trp Phe Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 839

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 839

Ser Arg Leu Tyr Ser Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 840

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 840

Gly Val Thr Phe Ser Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 841

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 841

Ser Ile Val Trp Ser Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 842

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 842

Ser Arg Asp Leu Val Gln Pro Tyr Ala Leu Pro Leu

1 5 10

<210> 843

<211> 17

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 843

His Trp Gly His Val Tyr Trp Gln Pro Tyr Ser Val Gln Asp Asp Leu
1 5 10 15

Gly

<210> 844

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 844

Ser Trp His Ser Val Tyr Trp Gln Pro Tyr Ser Val Gln Ser Val Pro
1 5 10 15

Glu

<210> 845

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 845

Trp Arg Asp Ser Val Tyr Trp Gln Pro Tyr Ser Val Gln Pro Glu Ser
1 5 10 15

Ala

<210> 846

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 846

Thr Trp Asp Ala Val Tyr Trp Gln Pro Tyr Ser Val Gln Lys Trp Leu
1 5 10 15

Asp

<210> 847

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 847

Thr Pro Pro Trp Val Tyr Trp Gln Pro Tyr Ser Val Gln Ser Leu Asp
1 5 10 15

Pro

<210> 848

<211> 17

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 848

Tyr Trp Ser Ser Val Tyr Trp Gln Pro Tyr Ser Val Gln Ser Val His
1 5 10 15

Ser

<210> 849

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 849

Tyr Trp Tyr Gln Pro Tyr Ala Leu Gly Leu
1 5 10

<210> 850

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 850

Tyr Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 851

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 851

Glu Trp Ile Gln Pro Tyr Ala Thr Gly Leu
1 5 10

<210> 852

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 852

Asn Trp Glu Gln Pro Tyr Ala Lys Pro Leu
1 5 10

<210> 853

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 853

Ala Phe Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 854

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 854

Phe Leu Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10

<210> 855

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 855

Val Cys Lys Gln Pro Tyr Leu Glu Trp Cys
1 5 10

<210> 856

<211> 21

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 856

Glu Thr Pro Phe Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15Tyr Ala Leu Pro Leu
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<210> 857

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 857

Gln Gly Trp Leu Thr Trp Gln Asp Ser Val Asp Met Tyr Trp Gln Pro
1 5 10 15Tyr Ala Leu Pro Leu
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<210> 858

<211> 21

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 858

Phe Ser Glu Ala Gly Tyr Thr Trp Pro Glu Asn Thr Tyr Trp Gln Pro
1 5 10 15Tyr Ala Leu Pro Leu
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<210> 859

<211> 21

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 859

Thr Glu Ser Pro Gly Gly Leu Asp Trp Ala Lys Ile Tyr Trp Gln Pro
1 5 10 15Tyr Ala Leu Pro Leu
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<210> 860
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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 860

Asp Gly Tyr Asp Arg Trp Arg Gln Ser Gly Glu Arg Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
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<210> 861
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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 861

Thr Ala Asn Val Ser Ser Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
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<210> 862
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<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 862

Ser Val Gly Glu Asp His Asn Phe Trp Thr Ser Glu Tyr Trp Gln Pro

1 5 10 15
Tyr Ala Leu Pro Leu
20

<210> 863
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<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 863
Met Asn Asp Gln Thr Ser Glu Val Ser Thr Phe Pro Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 864
<211> 21
<212> PRT
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<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 864
Ser Trp Ser Glu Ala Phe Glu Gln Pro Arg Asn Leu Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
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<210> 865
<211> 21
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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 865

Gln Tyr Ala Glu Pro Ser Ala Leu Asn Asp Trp Gly Tyr Trp Gln Pro
1 5 10 15Tyr Ala Leu Pro Leu
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<210> 866

<211> 21

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 866

Asn Gly Asp Trp Ala Thr Ala Asp Trp Ser Asn Tyr Tyr Trp Gln Pro
1 5 10 15Tyr Ala Leu Pro Leu
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<210> 867

<211> 15

<212> PRT

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 867

Thr His Asp Glu His Ile Tyr Trp Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 868

<211> 21

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 868

Met Leu Glu Lys Thr Tyr Thr Thr Trp Thr Pro Gly Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
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<210> 869

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 869

Trp Ser Asp Pro Leu Thr Arg Asp Ala Asp Leu Tyr Trp Gln Pro Tyr
1 5 10 15

Ala Leu Pro Leu
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<210> 870

<211> 21

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 870

Ser Asp Ala Phe Thr Thr Gln Asp Ser Gln Ala Met Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu

20

<210> 871
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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 871
Gly Asp Asp Ala Ala Trp Arg Thr Asp Ser Leu Thr Tyr Trp Gln Pro
1 5 10 15
Tyr Ala Leu Pro Leu
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<210> 872
<211> 21
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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 872
Ala Ile Ile Arg Gln Leu Tyr Arg Trp Ser Glu Met Tyr Trp Gln Pro
1 5 10 15
Tyr Ala Leu Pro Leu
20

<210> 873
<211> 21
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<220>
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PEPTIDE

<400> 873

Glu Asn Thr Tyr Ser Pro Asn Trp Ala Asp Ser Met Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 874

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 874

Met Asn Asp Gln Thr Ser Glu Val Ser Thr Phe Pro Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 875

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 875

Ser Val Gly Glu Asp His Asn Phe Trp Thr Ser Glu Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 876

<211> 21

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 876

Gln Thr Pro Phe Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
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<210> 877

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 877

Glu Asn Pro Phe Thr Trp Gln Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 878

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 878

Val Thr Pro Phe Thr Trp Glu Asp Ser Asn Val Phe Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu

20

<210> 879
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 879
Gln Ile Pro Phe Thr Trp Glu Gln Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15
Tyr Ala Leu Pro Leu
20

<210> 880
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 880
Gln Ala Pro Leu Thr Trp Gln Glu Ser Ala Ala Tyr Tyr Trp Gln Pro
1 5 10 15
Tyr Ala Leu Pro Leu
20

<210> 881
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 881

Glu Pro Thr Phe Thr Trp Glu Glu Ser Lys Ala Thr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 882

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 882

Thr Thr Thr Leu Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 883

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 883

Glu Ser Pro Leu Thr Trp Glu Glu Ser Ser Ala Leu Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 884

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 884

Glu Thr Pro Leu Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 885

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 885

Glu Ala Thr Phe Thr Trp Ala Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 886

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 886

Glu Ala Leu Phe Thr Trp Lys Glu Ser Thr Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu

20

<210> 887

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 887

Ser Thr Pro Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro Tyr
1 5 10 15Ala Leu Pro Leu
20

<210> 888

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 888

Glu Thr Pro Phe Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15Tyr Ala Leu Pro Leu
20

<210> 889

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 889

Lys Ala Pro Phe Thr Trp Glu Glu Ser Gln Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 890

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 890

Ser Thr Ser Phe Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 891

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 891

Asp Ser Thr Phe Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 892

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 892

Tyr Ile Pro Phe Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 893

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 893

Gln Thr Ala Phe Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 894

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 894

Glu Thr Leu Phe Thr Trp Glu Glu Ser Asn Ala Thr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu

20

<210> 895

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 895

Val Ser Ser Phe Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15Tyr Ala Leu Pro Leu
20

<210> 896

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 896

Gln Pro Tyr Ala Leu Pro Leu
1 5

<210> 897

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa is a phosphotyrosyl residue

<220>

<223> At position 2, Xaa is a 1-naphthylalanyl residue

<220>

<223> At position 6, Xaa is an azetidine residue

<400> 897

Xaa Xaa Pro Tyr Gln Xaa Tyr Ala Leu Pro Leu
1 5 10

<210> 898

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 898

Thr Ala Asn Val Ser Ser Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 899

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 899

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 900

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 900

| | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Tyr | Trp | Gln | Xaa | Tyr | Ala | Leu | Pro | Leu |
| 1 | | | | 5 | | | | 10 | | | | 15 | | |

<210> 901

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 901

| | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Tyr | Tyr | Gln | Xaa | Tyr | Ala | Leu | Pro | Leu |
| 1 | | | | 5 | | | | 10 | | | | 15 | | |

<210> 902

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 902

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Glu | Thr | Pro | Phe | Thr | Trp | Glu | Glu | Ser | Asn | Ala | Tyr | Tyr | Trp | Gln | Pro |
| 1 | | | | 5 | | | | 10 | | | | | 15 | | |

Tyr Ala Leu Pro Leu

20

<210> 903
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 13, Xaa is an azetidine residue

<400> 903
Phe Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Xaa Tyr Ala Leu
1 5 10 15
Pro Leu

<210> 904
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 904
Ala Asp Val Leu Tyr Trp Gln Pro Tyr Ala Pro Val Thr Leu Trp Val
1 5 10 15

<210> 905
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 905

Gly Asp Val Ala Glu Tyr Trp Gln Pro Tyr Ala Leu Pro Leu Thr Ser
1 5 10 15

Leu

<210> 906

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 906

Ser Trp Thr Asp Tyr Gly Tyr Trp Gln Pro Tyr Ala Leu Pro Ile Ser
1 5 10 15

Gly Leu

<210> 907

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 4, Xaa is prolyl or an azetidine
residue

<220>

<223> At position 6, Xaa is S, A, V or L

<400> 907

Xaa Xaa Gln Xaa Tyr Xaa Xaa Xaa
1 5

<210> 908

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa is Y, W or F

<220>

<223> At position 4, Xaa is prolyl or an azetidine
residue

<220>

<223> At position 6, Xaa is S, A, V or L

<400> 908

Xaa Xaa Gln Xaa Tyr Xaa Xaa Xaa

1

5

<210> 909

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa is Y, W or F

<220>

<223> At position 2, Xaa is E, F, V, W or Y

<220>

<223> At position 4, Xaa is prolyl or an azetidine
residue

<220>

<223> At position 6, Xaa is S, A, V or L

<220>

<223> At position 7, Xaa is M, F, V, R, Q, K, T, S, D,
L, I or E

<220>

<223> At position 8, Xaa is E, L, W, V, H, I, G, A, D,
L, Y, N, Q or P

<400> 909

Xaa Xaa Gln Xaa Tyr Xaa Xaa Xaa
1 5

<210> 910

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa is V, L, I, E, P, G, Y, M, T or
D

<220>

<223> At position 2, Xaa is Y, W or F

<220>

<223> At position 3, Xaa is E, F, V, W or Y

<220>

<223> At position 5, Xaa is prolyl or an azetidine
residue

<220>

<223> At position 7, Xaa is S, A, V or L

<220>

<223> At position 8, Xaa is M, F, V, R, Q, K, T, S, D,
L, I or E

<220>

<223> At position 9, Xaa is E, L, W, V, H, I, G, A, D,
L, Y, N, Q or P

<400> 910

Xaa Xaa Xaa Gln Xaa Tyr Xaa Xaa Xaa

1

5

<210> 911

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 911

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro Tyr Ala Leu Pro Leu

1

5

10

15

<210> 912

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 912

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr Ala Leu Pro Leu

1

5

10

15

<210> 913

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 913

Phe Glu Trp Thr Pro Gly Trp Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 914

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 914

Phe Glu Trp Thr Pro Gly Trp Tyr Gln Xaa Tyr Ala Leu Pro Leu
1 5 10 15

<210> 915

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 915

Phe Glu Trp Thr Pro Gly Tyr Tyr Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 916

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 916

| | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Tyr | Tyr | Gln | Xaa | Tyr | Ala | Leu | Pro | Leu |
| 1 | | | | 5 | | | | 10 | | | | 15 | | |

<210> 917

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa is A, D, E, F, G, K, Q, S, T, V
or Y

<220>

<223> At position 2, Xaa is A, D, G, I, N, P, S, T, V or
W

<220>

<223> At position 3, Xaa is A, D, G, L, N, P, S, T, W or
Y

<220>

<223> At position 4, Xaa is A, D, E, F, L, N, R, V or Y

<220>

<223> At position 5, Xaa is A, D, E, Q, R, S or T

<220>

<223> At position 6, Xaa is H, I, L, P, S, T or W

<220>

<223> At position 7, Xaa is A, E, F, K, N, Q, R, S or Y

<220>

<223> At position 8, Xaa is D, E, F, Q, R, T or W

<220>

<223> At position 9, Xaa is A, D, P, S, T or W

<220>

<223> At position 10, Xaa is A, D, G, K, N, Q, S or T

<220>

<223> At position 11, Xaa is A, E, L, P, S, T, V or Y

<220>

<223> At position 12, Xaa is V, L, I, E, P, G, Y, M, T
or D

<220>

<223> At position 13, Xaa is Y, W or F

<220>

<223> At position 14, Xaa is E, F, V, W or Y

<220>

<223> At position 16, Xaa is P or an azetidine residue

<220>

<223> At position 18, Xaa is S, A, V or L

<220>

<223> At position 19, Xaa is M, F, V, R, Q, K, T, S, D,
L, I or E

<220>

<223> At position 20, Xaa is Q or P

<400> 917

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Gln | Xaa |
| 1 | | | | 5 | | | | | | 10 | | | | | 15 | |

| | | | | |
|-----|-----|-----|-----|-----|
| Tyr | Xaa | Xaa | Xaa | Leu |
| | | | | 20 |

<210> 918

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: IL-1 ANTAGONIST
PEPTIDE

<400> 918

Thr Ala Asn Val Ser Ser Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 919

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 919

Ser Trp Thr Asp Tyr Gly Tyr Trp Gln Pro Tyr Ala Leu Pro Ile Ser
1 5 10 15

Gly Leu

<210> 920

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 920

Glu Thr Pro Phe Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 921

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 921

Glu Asn Thr Tyr Ser Pro Asn Trp Ala Asp Ser Met Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 922

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 922

Ser Val Gly Glu Asp His Asn Phe Trp Thr Ser Glu Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 923

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 923

Asp Gly Tyr Asp Arg Trp Arg Gln Ser Gly Glu Arg Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 924
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 924
Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro Tyr Ala Leu Pro Leu
1 5 10 15

<210> 925
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 925
Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro Tyr Asn His
1 5 10

<210> 926
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 10, Xaa is an azetidine residue

<400> 926
Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr Asn His
1 5 10

<210> 927

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 927

Glu Trp Thr Pro Gly Tyr Trp Gln Pro Tyr Asn His
1 5 10

<210> 928

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 928

Phe Glu Trp Thr Pro Gly Trp Tyr Gln Xaa Tyr
1 5 10

<210> 929

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 929

Ala Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr

1

5

10

<210> 930

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 930

Phe Ala Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr

1

5

10

<210> 931

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 931

Phe Glu Ala Thr Pro Gly Tyr Trp Gln Xaa Tyr

1

5

10

<210> 932

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 932

Phe Glu Trp Ala Pro Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 933

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 933

Phe Glu Trp Thr Ala Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 934

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 934

Phe Glu Trp Thr Pro Ala Tyr Trp Gln Xaa Tyr
1 5 10

<210> 935
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 10, Xaa is an azetidine residue

<400> 935
Phe Glu Trp Thr Pro Gly Ala Trp Gln Xaa Tyr
1 5 10

<210> 936
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 10, Xaa is an azetidine residue

<400> 936
Phe Glu Trp Thr Pro Gly Tyr Ala Gln Xaa Tyr
1 5 10

<210> 937
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 10, Xaa is an azetidine residue

<400> 937

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Ala
1 5 10

<210> 938

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 938

Phe Glu Trp Thr Gly Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 939

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, D amino acid residue

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 939

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 940

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 940

| | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Gly | Tyr | Trp | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | 10 | |

<210> 941

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, Xaa is a pipecolic acid residue

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 941

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Xaa | Gly | Tyr | Trp | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 942

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 6, Xaa is an aminoisobutyric acid
residue

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 942

Phe Glu Trp Thr Pro Xaa Tyr Trp Gln Xaa Tyr

1

5

10

<210> 943

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 6, Xaa is a sarcosine residue

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 943

Phe Glu Trp Thr Pro Xaa Trp Tyr Gln Xaa Tyr

1

5

10

<210> 944

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, Xaa is a sarcosine residue

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 944

Phe Glu Trp Thr Xaa Gly Tyr Trp Gln Xaa Tyr

1 5 10

<210> 945

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 945

Phe Glu Trp Thr Pro Asn Tyr Trp Gln Xaa Tyr
1 5 10

<210> 946

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, D amino acid residue

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 946

Phe Glu Trp Thr Pro Val Tyr Trp Gln Xaa Tyr
1 5 10

<210> 947

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 947

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Val | Pro | Tyr | Trp | Gln | Xaa | Tyr |
| 1 | | | | | 5 | | | | 10 | |

<210> 948

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa is acetylated phe

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 948

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Trp | Tyr | Gln | Xaa | Tyr |
| 1 | | | | | 5 | | | | 10 | |

<210> 949

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa is acetylated phe

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 949

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 950

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=1-naphthylalanine

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 950

Xaa Glu Trp Thr Pro Gly Tyr Tyr Gln Xaa Tyr
1 5 10

<210> 951

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 951

Tyr Glu Trp Thr Pro Gly Tyr Tyr Gln Xaa Tyr
1 5 10

<210> 952

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 952

Phe Glu Trp Val Pro Gly Tyr Tyr Gln Xaa Tyr
1 5 10

<210> 953

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 953

Phe Glu Trp Thr Pro Gly Tyr Tyr Gln Xaa Tyr
1 5 10

<210> 954

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 954

Phe Glu Trp Thr Pro Ser Tyr Tyr Gln Xaa Tyr

1 5 10

<210> 955

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 955

Phe Glu Trp Thr Pro Asn Tyr Tyr Gln Xaa Tyr
1 5 10

<210> 956

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, Xaa=naphthylalanine

<400> 956

Ser His Leu Tyr Xaa Gln Pro Tyr Ser Val Gln Met
1 5 10

<210> 957

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, Xaa=naphthylalanine

<400> 957

Thr Leu Val Tyr Xaa Gln Pro Tyr Ser Leu Gln Thr
1 5 10

<210> 958

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, Xaa=naphthylalanine

<400> 958

Arg Gly Asp Tyr Xaa Gln Pro Tyr Ser Val Gln Ser
1 5 10

<210> 959

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, Xaa=naphthylalanine

<400> 959

Asn Met Val Tyr Xaa Gln Pro Tyr Ser Ile Gln Thr
1 5 10

<210> 960

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 960

Val Tyr Trp Gln Pro Tyr Ser Val Gln

1

5

<210> 961

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 3, Xaa=naphthylalanine

<400> 961

Val Tyr Xaa Gln Pro Tyr Ser Val Gln

1

5

<210> 962

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 7, Xaa is an azetidine residue

<400> 962

Thr Phe Val Tyr Trp Gln Xaa Tyr Ala Leu Pro Leu

1

5

10

<210> 963
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 10, Xaa is an azetidine residue

<220>
<223> At position 11, Xaa =p-benzoyl-L-phenylalanine

<400> 963
Phe Glu Trp Thr Pro Gly Tyr Tyr Gln Xaa Xaa
1 5 10

<210> 964
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 1, Xaa=acetylated phe

<220>
<223> At position 10, Xaa is an azetidine residue

<220>
<223> At position 11, Xaa=p-benzoyl-L-phenylalanine

<400> 964
Xaa Glu Trp Thr Pro Gly Tyr Tyr Gln Xaa Xaa
1 5 10

<210> 965
<211> 11

<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 8, Xaa=p-benzoyl-L-phenylalanine

<220>
<223> At position 10, Xaa is an azetidine residue

<400> 965
Phe Glu Trp Thr Pro Gly Tyr Xaa Gln Xaa Tyr
1 5 10

<210> 966
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 1, Xaa=acetylated phe

<220>
<223> At position 8, Xaa=p-benzoyl-L-phenylalanine

<220>
<223> At position 10, Xaa is an azetidine residue

<400> 966
Phe Glu Trp Thr Pro Gly Tyr Xaa Gln Xaa Tyr
1 5 10

<210> 967
<211> 11
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 7, Xaa=p-benzoyl-L-phenylalanine

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 967

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Xaa | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 968

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 7, Xaa=p-benzoyl-L-phenylalanine

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 968

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Xaa | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 969

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 3, Xaa=p-benzoyl-L-phenylalanine

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 969

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Xaa | Thr | Pro | Gly | Tyr | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 970

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 3, Xaa=p-benzoyl-L-phenylalanine

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 970

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Xaa | Thr | Pro | Gly | Tyr | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 971

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=p-benzoyl-L-phenylalanine

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 971

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Xaa | Glu | Trp | Thr | Pro | Gly | Tyr | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 972

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated
p-benzoyl-L-phenylalanine

<220>

<223> At position 10, Xaa is an azetidine residue

<400> 972

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Xaa | Glu | Trp | Thr | Pro | Gly | Tyr | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 973

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 973

| | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Tyr | Trp | Gln | Pro | Tyr | Ser | Val | Gln |
| 1 | | | | 5 | | | | |

<210> 974
<211> 12
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 974

Arg Leu Val Tyr Trp Gln Pro Tyr Ser Val Gln Arg
1 5 10

<210> 975
<211> 12
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 5, Xaa=naphthylalanine

<400> 975

Arg Leu Val Tyr Xaa Gln Pro Tyr Ser Val Gln Arg
1 5 10

<210> 976
<211> 12
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 976

Arg Leu Asp Tyr Trp Gln Pro Tyr Ser Val Gln Arg
1 5 10

<210> 977
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 977
Arg Leu Val Trp Phe Gln Pro Tyr Ser Val Gln Arg
1 5 10

<210> 978
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 978
Arg Leu Val Tyr Trp Gln Pro Tyr Ser Ile Gln Arg
1 5 10

<210> 979
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 1, Xaa=D or Y

<220>
<223> At position 3, Xaa=D or S

<220>

<223> At position 4, Xaa=S, T or A

<220>

<223> At position 5, Xaa=S or W

<220>

<223> At position 6, Xaa=S or Y

<220>

<223> At position 7, Xaa=D, Q, E or V

<220>

<223> At position 8, Xaa=N, S, K, H or W

<220>

<223> At position 9, Xaa=F or L

<220>

<223> At position 10, Xaa=D, N, S or L

<220>

<223> At position 11, Xaa=L, I, Q, M or A

<400> 979

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Xaa | Asn | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
| 1 | | | 5 | | | | | | 10 | |

<210> 980

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 980

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asp | Asn | Ser | Ser | Trp | Tyr | Asp | Ser | Phe | Leu | Leu |
| 1 | | | | 5 | | | | | 10 | |

<210> 981

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 981

Asp Asn Thr Ala Trp Tyr Glu Ser Phe Leu Ala
1 5 10

<210> 982

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 982

Asp Asn Thr Ala Trp Tyr Glu Asn Phe Leu Leu
1 5 10

<210> 983

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 983

Pro Ala Arg Glu Asp Asn Thr Ala Trp Tyr Asp Ser Phe Leu Ile Trp
1 5 10 15

Cys

<210> 984

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 984

Thr Ser Glu Tyr Asp Asn Thr Thr Trp Tyr Glu Lys Phe Leu Ala Ser
1 5 10 15

Gln

<210> 985

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 985

Ser Gln Ile Pro Asp Asn Thr Ala Trp Tyr Gln Ser Phe Leu Leu His
1 5 10 15

Gly

<210> 986

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 986

Ser Pro Phe Ile Asp Asn Thr Ala Trp Tyr Glu Asn Phe Leu Leu Thr
1 5 10 15

Tyr

<210> 987
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 987
Glu Gln Ile Tyr Asp Asn Thr Ala Trp Tyr Asp His Phe Leu Leu Ser
1 5 10 15

Tyr

<210> 988
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 988
Thr Pro Phe Ile Asp Asn Thr Ala Trp Tyr Glu Asn Phe Leu Leu Thr
1 5 10 15

Tyr

<210> 989
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 989

Thr Tyr Thr Tyr Asp Asn Thr Ala Trp Tyr Glu Arg Phe Leu Met Ser
1 5 10 15

Tyr

<210> 990

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 990

Thr Met Thr Gln Asp Asn Thr Ala Trp Tyr Glu Asn Phe Leu Leu Ser
1 5 10 15

Tyr

<210> 991

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 991

Thr Ile Asp Asn Thr Ala Trp Tyr Ala Asn Leu Val Gln Thr Tyr Pro
1 5 10 15

Gln

<210> 992

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 992

Thr Ile Asp Asn Thr Ala Trp Tyr Glu Arg Phe Leu Ala Gln Tyr Pro
1 5 10 15

Asp

<210> 993

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 993

His Ile Asp Asn Thr Ala Trp Tyr Glu Asn Phe Leu Leu Thr Tyr Thr
1 5 10 15

Pro

<210> 994

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 994

Ser Gln Asp Asn Thr Ala Trp Tyr Glu Asn Phe Leu Leu Ser Tyr Lys
1 5 10 15

Ala

<210> 995
<211> 17
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 995

Gln Ile Asp Asn Thr Ala Trp Tyr Glu Arg Phe Leu Leu Gln Tyr Asn
1 5 10 15

Ala

<210> 996
<211> 17
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 996

Asn Gln Asp Asn Thr Ala Trp Tyr Glu Ser Phe Leu Leu Gln Tyr Asn
1 5 10 15

Thr

<210> 997
<211> 17
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 997

Thr Ile Asp Asn Thr Ala Trp Tyr Glu Asn Phe Leu Leu Asn His Asn
1 5 10 15

Leu

<210> 998

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 998

His Tyr Asp Asn Thr Ala Trp Tyr Glu Arg Phe Leu Gln Gln Gly Trp
1 5 10 15

His

<210> 999

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 999

Glu Thr Pro Phe Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 1000

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 1000

Tyr Ile Pro Phe Thr Trp Glu Glu Ser Asn Ala Tyr Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 1001

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 1001

Asp Gly Tyr Asp Arg Trp Arg Gln Ser Gly Glu Arg Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 1002

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=phosphotyrosine

<220>

<223> At position 2, Xaa=naphthylalanine

<220>

<223> At position 3, Xaa=phosphotyrosine

<220>

<223> At position 5, Xaa is an azetidine residue

<400> 1002

Xaa Xaa Xaa Gln Xaa Tyr Ala Leu Pro Leu

1

5

10

<210> 1003

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 1003

Thr Ala Asn Val Ser Ser Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro

1

5

10

15

Tyr Ala Leu Pro Leu

20

<210> 1004

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa=azetidine

<400> 1004

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr Ala Leu Pro Leu

1

5

10

15

<210> 1005

<211> 19
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<400> 1005

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Tyr | Trp | Gln | Pro | Tyr | Ala | Leu | Pro | Leu | Ser |
| 1 | | | | 5 | | | | 10 | | | | | 15 | | |

Asp Asn His

<210> 1006
<211> 15
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa=azetidine

<400> 1006

| | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Gly | Tyr | Tyr | Gln | Xaa | Tyr | Ala | Leu | Pro | Leu |
| 1 | | | | 5 | | | | 10 | | | | | 15 | |

<210> 1007
<211> 11
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa=azetidine

<400> 1007

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 1008

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 10, Xaa=azetidine

<400> 1008

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 1009

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 10, Xaa=azetidine

<400> 1009

Phe Glu Trp Thr Pro Gly Trp Tyr Gln Xaa Tyr
1 5 10

<210> 1010

<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 1, Xaa=acetylated phe

<220>
<223> At position 10, Xaa=azetidine

<400> 1010
Phe Glu Trp Thr Pro Gly Tyr Tyr Gln Xaa Tyr
1 5 10

<210> 1011
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>
<223> At position 1, Xaa=acetylated phe

<220>
<223> At position 10, Xaa=azetidine

<400> 1011
Phe Glu Trp Thr Pro Ala Tyr Trp Gln Xaa Tyr
1 5 10

<210> 1012
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:IL-1 ANTAGONIST

PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 10, Xaa=azetidine

<400> 1012

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Ala | Trp | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 1013

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 10, Xaa=azetidine

<400> 1013

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Ala | Tyr | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 1014

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa=azetidine

<400> 1014

Phe Glu Trp Thr Pro Gly Tyr Tyr Gln Xaa Tyr Ala Leu Pro Leu
1 5 10 15

<210> 1015

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa=azetidine

<400> 1015

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr Ala Leu Pro Leu
1 5 10 15

<210> 1016

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 10, Xaa=azetidine

<400> 1016

Phe Glu Trp Thr Pro Gly Trp Tyr Gln Xaa Tyr Ala Leu Pro Leu
1 5 10 15

<210> 1017

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST

PEPTIDE

<400> 1017

Thr Ala Asn Val Ser Ser Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 1018

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 10, Xaa=azetidine

<400> 1018

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Xaa Tyr
1 5 10

<210> 1019

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 10, Xaa=azetidine

<400> 1019

Phe Glu Trp Thr Pro Gly Trp Tyr Gln Xaa Tyr
1 5 10

<210> 1020

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 10, Xaa=azetidine

<400> 1020

Phe Glu Trp Thr Pro Gly Tyr Tyr Gln Xaa Tyr
1 5 10

<210> 1021

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 6, D amino acid residue

<220>

<223> At position 10, Xaa=azetidine

<400> 1021

Phe Glu Trp Thr Pro Ala Tyr Trp Gln Xaa Tyr
1 5 10

<210> 1022

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 6, D amino acid residue

<220>

<223> At position 10, Xaa=azetidine

<400> 1022

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Ala | Trp | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 1023

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PEPTIDE

<220>

<223> At position 1, Xaa=acetylated phe

<220>

<223> At position 6, D amino acid residue

<220>

<223> At position 10, Xaa=azetidine

<400> 1023

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Glu | Trp | Thr | Pro | Ala | Tyr | Tyr | Gln | Xaa | Tyr |
| 1 | | | | 5 | | | | | 10 | |

<210> 1024

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC
PEPTIDE

<400> 1024

Gly Gly Leu Tyr Leu Cys Arg Phe Gly Pro Val Thr Trp Asp Cys Gly
1 5 10 15

Tyr Lys Gly Gly
20

<210> 1025

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC
PEPTIDE

<400> 1025

Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
1 5 10 15

Pro Gln Gly Gly
20

<210> 1026

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO-MIMETIC
PEPTIDE

<400> 1026

Gly Gly Asp Tyr His Cys Arg Met Gly Pro Leu Thr Trp Val Cys Lys
1 5 10 15

Pro Leu Gly Gly
20

<210> 1027

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC
PEPTIDE

<400> 1027

Cys Gly Arg Glu Cys Pro Arg Leu Cys Gln Ser Ser Cys
1 5 10

<210> 1028

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC
PEPTIDE

<400> 1028

Cys Asn Gly Arg Cys Val Ser Gly Cys Ala Gly Arg Cys
1 5 10

<210> 1029

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC
PEPTIDE

<400> 1029

Val Gly Asn Tyr Met Cys His Phe Gly Pro Ile Thr Trp Val Cys Arg
1 5 10 15

Pro Gly Gly Gly
20

<210> 1030

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC
PEPTIDE

<400> 1030

Gly Gly Val Tyr Ala Cys Arg Met Gly Pro Ile Thr Trp Val Cys Ser
1 5 10 15

Pro Leu Gly Gly
20

<210> 1031

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VEGF ANTAGONIST
PEPTIDE

<400> 1031

Cys Asn Gly Arg Cys
1 5

<210> 1032

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TPO MIMETIC

<400> 1032

Cys Asp Cys Arg Gly Asp Cys Phe Cys

1

5

<210> 1033

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC

<400> 1033

Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Gly Gly

1

5

10

15

Gly Gly Gly Phe

20

<210> 1034

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC

<400> 1034

Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys

1

5

10

15

Pro Gln Gly Gly Gly Gly Gly Gly Phe

20

25

<210> 1035

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC

<400> 1035

Val Gly Asn Tyr Met Ala His Met Gly Pro Ile Thr Trp Val Cys Arg
1 5 10 15

Pro Gly Gly

<210> 1036

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC

<400> 1036

Gly Gly Thr Tyr Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
1 5 10 15

Pro Gln

<210> 1037

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC

<400> 1037

Gly Gly Leu Tyr Ala Cys His Met Gly Pro Met Thr Trp Val Cys Gln
1 5 10 15

Pro Leu Arg Gly
20

<210> 1038

<211> 22

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC

<400> 1038

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Thr | Ile | Ala | Gln | Tyr | Ile | Cys | Tyr | Met | Gly | Pro | Glu | Thr | Trp | Glu | Cys |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

| | | | | | |
|-----|-----|-----|-----|-----|-----|
| Arg | Pro | Ser | Pro | Lys | Ala |
| | | | | 20 | |

<210> 1039

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC

<400> 1039

| | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Tyr | Ser | Cys | His | Phe | Gly | Pro | Leu | Thr | Trp | Val | Cys | Lys |
| 1 | | | | 5 | | | | | 10 | | | |

<210> 1040

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC
PEPTIDE

<400> 1040

| | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Tyr | Cys | His | Phe | Gly | Pro | Leu | Thr | Trp | Val | Cys |
| 1 | | | | 5 | | | | | 10 | |

<210> 1041

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC
PEPTIDE

<400> 1041

Ser Cys His Phe Gly Pro Leu Thr Trp Val Cys Lys
1 5 10

<210> 1042

<211> 40

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC
PEPTIDE

<400> 1042

Ala Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Gly
1 5 10 15

Pro Xaa Xaa Xaa Xaa Xaa Xaa Thr Trp Xaa Xaa Xaa Xaa Xaa Xaa Xaa
20 25 30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
35 40

<210> 1043

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:EPO MIMETIC
PEPTIDE

<400> 1043

Asp Leu Xaa Xaa Leu
1 5

<210> 1044

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 1044

Arg Thr Asp Leu Asp Ser Leu Arg Thr Tyr Thr Leu
1 5 10

<210> 1045

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF ANTAGONIST

<400> 1045

Phe Gly Gly Gly Gly Gly Asp Phe Leu Pro His Tyr Lys Asn Thr Ser
1 5 10 15

Leu Gly His Arg Pro
20

<210> 1046

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF ANTAGONIST

<400> 1046

Asp Phe Leu Pro His Tyr Lys Asn Thr Ser Leu Gly His Arg Pro Gly
1 5 10 15

Gly Gly Gly Gly Phe
20

<210> 1047

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST

<400> 1047

Phe Gly Gly Gly Gly Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro
1 5 10 15

Tyr Ala Leu Pro Leu
20

<210> 1048

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST

<400> 1048

Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro Tyr Ala Leu Pro Leu Gly
1 5 10 15

Gly Gly Gly Gly Phe
20

<210> 1049

<211> 25

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VEGF ANTAGONIST

<400> 1049

Phe Gly Gly Gly Gly Gly Val Glu Pro Asn Cys Asp Ile His Val Met
1 5 10 15

Trp Glu Trp Glu Cys Phe Glu Arg Leu
20 25

<210> 1050

<211> 25

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VEGF ANTAGONIST

<400> 1050

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Glu | Pro | Asn | Cys | Asp | Ile | His | Val | Met | Trp | Glu | Trp | Glu | Cys | Phe |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

| | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Glu | Arg | Leu | Gly | Gly | Gly | Gly | Gly | Phe |
| | | | 20 | | | | | 25 |

<210> 1051

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MMP INHIBITOR

<400> 1051

| | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Gly | Gly | Gly | Gly | Cys | Thr | Thr | His | Trp | Gly | Phe | Thr | Leu | Cys |
| 1 | | | | 5 | | | | 10 | | | | | 15 | |

<210> 1052

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MMP INHIBITOR

<400> 1052

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Thr | Thr | His | Trp | Gly | Phe | Thr | Leu | Cys | Gly | Gly | Gly | Gly | Gly | Phe |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

<210> 1053

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 1053

Arg Thr Asp Leu Asp Ser Leu Arg Thr Tyr
1 5 10

<210> 1054

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 1054

Arg Thr Asp Leu Asp Ser Leu Arg Thr
1 5

<210> 1055

<211> 757

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TNF-ALPHA
INHIBITOR

<220>

<221> CDS

<222> (4)..(747)

<400> 1055

cat atg gac aaa act cac aca tgt cca cct tgt cca gct ccg gaa ctc 48
Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
1 5 10 15ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac acc 96
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr

| | 20 | 25 | 30 | |
|---|-----|-----|-----|-----|
| ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac gtg | | | | 144 |
| Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val | | | | |
| | 35 | 40 | 45 | |
| agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc gtg | | | | 192 |
| Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val | | | | |
| | 50 | 55 | 60 | |
| gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac agc | | | | 240 |
| Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser | | | | |
| | 65 | 70 | 75 | |
| acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg ctg | | | | 288 |
| Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu | | | | |
| | 80 | 85 | 90 | 95 |
| aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca gcc | | | | 336 |
| Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala | | | | |
| | 100 | 105 | 110 | |
| ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca | | | | 384 |
| Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro | | | | |
| | 115 | 120 | 125 | |
| cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac cag | | | | 432 |
| Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln | | | | |
| | 130 | 135 | 140 | |
| gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc gcc | | | | 480 |
| Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala | | | | |
| | 145 | 150 | 155 | |
| gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc acg | | | | 528 |
| Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr | | | | |
| | 160 | 165 | 170 | 175 |
| cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc | | | | 576 |
| Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu | | | | |
| | 180 | 185 | 190 | |
| acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc | | | | 624 |
| Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser | | | | |
| | 195 | 200 | 205 | |
| gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc | | | | 672 |
| Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser | | | | |

210 215 220

ctg tct ccg ggt aaa ggt gga ggt ggt ggt gac ttc ctg ccg cac tac 720
 Leu Ser Pro Gly Lys Gly Gly Gly Gly Gly Asp Phe Leu Pro His Tyr
 225 230 235

aaa aac acc tct ctg ggt cac cgt ccg taatggatcc 757
 Lys Asn Thr Ser Leu Gly His Arg Pro
 240 245

<210> 1056

<211> 248

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc-TNF-ALPHA
 INHIBITOR

<400> 1056

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
 1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
 20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
 65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
 85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
 100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
 115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
 130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
 145 150 155 160

395

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
 165 170 175
 Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
 180 185 190
 Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
 195 200 205
 Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
 210 215 220
 Ser Pro Gly Lys Gly Gly Gly Gly Gly Asp Phe Leu Pro His Tyr Lys
 225 230 235 240
 Asn Thr Ser Leu Gly His Arg Pro
 245

<210> 1057

<211> 761

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ALPH
INHIBITOR Fc

<220>

<221> CDS

<222> (4)..(747)

<400> 1057

| | |
|---|-----|
| cat atg gac ttc ctg ccg cac tac aaa aac acc tct ctg ggt cac cgt | 48 |
| Met Asp Phe Leu Pro His Tyr Lys Asn Thr Ser Leu Gly His Arg | |
| 1 5 10 15 | |
| ccg ggt gga ggc ggt ggg gac aaa act cac aca tgt cca cct tgc cca | 96 |
| Pro Gly Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro | |
| 20 25 30 | |
| gca cct gaa ctc ctg ggg gga ccg tca gtt ttc ctc ttc ccc cca aaa | 144 |
| Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys | |
| 35 40 45 | |
| ccc aag gac acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg | 192 |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|------------|------|-----|-----|-----|-----|-----|-----|
| Pro | Lys | Asp | Thr | Leu | Met | Ile | Ser | Arg | Thr | Pro | Glu | Val | Thr | Cys | Val | |
| | | 50 | | | | | 55 | | | | | 60 | | | | |
| gtg | gtg | gac | gtg | agc | cac | gaa | gac | cct | gag | gtc | aag | ttc | aac | tgg | tac | 240 |
| Val | Val | Asp | Val | Ser | His | Glu | Asp | Pro | Glu | Val | Lys | Phe | Asn | Trp | Tyr | |
| | | 65 | | | | 70 | | | | | 75 | | | | | |
| gtg | gac | ggc | gtg | gag | gtg | cat | aat | gcc | aag | aca | aag | ccg | cgg | gag | gag | 288 |
| Val | Asp | Gly | Val | Glu | Val | His | Asn | Ala | Lys | Thr | Lys | Pro | Arg | Glu | Glu | |
| | 80 | | | | 85 | | | | 90 | | | | | 95 | | |
| cag | tac | aac | agc | acg | tac | cgt | gtg | gtc | agc | gtc | ctc | acc | gtc | ctg | cac | 336 |
| Gln | Tyr | Asn | Ser | Thr | Tyr | Arg | Val | Val | Ser | Val | Leu | Thr | Val | Leu | His | |
| | | | | 100 | | | | | 105 | | | | | 110 | | |
| cag | gac | tgg | ctg | aat | ggc | aag | gag | tac | aag | tgc | aag | gtc | tcc | aac | aaa | 384 |
| Gln | Asp | Trp | Leu | Asn | Gly | Lys | Glu | Tyr | Lys | Cys | Lys | Val | Ser | Asn | Lys | |
| | | | 115 | | | | | 120 | | | | | 125 | | | |
| gcc | ctc | cca | gcc | ccc | atc | gag | aaa | acc | atc | tcc | aaa | gcc | aaa | ggg | cag | 432 |
| Ala | Leu | Pro | Ala | Pro | Ile | Glu | Lys | Thr | Ile | Ser | Lys | Ala | Lys | Gly | Gln | |
| | | 130 | | | | | 135 | | | | | 140 | | | | |
| ccc | cga | gaa | cca | cag | gtg | tac | acc | ctg | ccc | cca | tcc | cgg | gat | gag | ctg | 480 |
| Pro | Arg | Glu | Pro | Gln | Val | Tyr | Thr | Leu | Pro | Pro | Ser | Arg | Asp | Glu | Leu | |
| | | 145 | | | | | 150 | | | | 155 | | | | | |
| acc | aag | aac | cag | gtc | agc | ctg | acc | tgc | ctg | gtc | aaa | ggc | ttc | tat | ccc | 528 |
| Thr | Lys | Asn | Gln | Val | Ser | Leu | Thr | Cys | Leu | Val | Lys | Gly | Phe | Tyr | Pro | |
| | | | | | 165 | | | | | 170 | | | | | 175 | |
| agc | gac | atc | gcc | gtg | gag | tgg | gag | agc | aat | ggg | cag | ccg | gag | aac | aac | 576 |
| Ser | Asp | Ile | Ala | Val | Glu | Trp | Glu | Ser | Asn | Gly | Gln | Pro | Glu | Asn | Asn | |
| | | | | 180 | | | | | 185 | | | | | 190 | | |
| tac | aag | acc | acg | cct | ccc | gtg | ctg | gac | tcc | gac | ggc | tcc | ttc | ttc | ctc | 624 |
| Tyr | Lys | Thr | Thr | Pro | Pro | Val | Leu | Asp | Ser | Asp | Gly | Ser | Phe | Phe | Leu | |
| | | | | 195 | | | | 200 | | | | | 205 | | | |
| tac | agc | aag | ctc | acc | gtg | gac | aag | agc | agg | tgg | cag | cag | ggg | aac | gtc | 672 |
| Tyr | Ser | Lys | Leu | Thr | Val | Asp | Lys | Ser | Arg | Trp | Gln | Gln | Gly | Asn | Val | |
| | | 210 | | | | | 215 | | | | | 220 | | | | |
| ttc | tca | tgc | tcc | gtg | atg | cat | gag | gct | ctg | cac | aac | cac | tac | acg | cag | 720 |
| Phe | Ser | Cys | Ser | Val | Met | His | Glu | Ala | Leu | His | Asn | His | Tyr | Thr | Gln | |
| | | 225 | | | | 230 | | | | | 235 | | | | | |
| aag | agc | ctc | tcc | ctg | tct | ccg | ggg | aaa | taatggatcc | gcgg | | | | | | 761 |

Lys Ser Leu Ser Leu Ser Pro Gly Lys
240 245

<210> 1058

<211> 248

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:TNF-ALPH
INHIBITOR Fc

<400> 1058

Met Asp Phe Leu Pro His Tyr Lys Asn Thr Ser Leu Gly His Arg Pro
1 5 10 15

Gly Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
20 25 30

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
35 40 45

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
50 55 60

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
65 70 75 80

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
85 90 95

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
100 105 110

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
115 120 125

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
130 135 140

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
145 150 155 160

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
165 170 175

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
180 185 190

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
 195 200 205

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
 210 215 220

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
 225 230 235 240

Ser Leu Ser Leu Ser Pro Gly Lys
 245

<210> 1059

<211> 763

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc IL-1
 ANTAGONIST

<220>

<221> CDS

<222> (4)..(747)

<400> 1059

| | |
|---|-----|
| cat atg gac aaa act cac aca tgt cca cct tgt cca gct ccg gaa ctc | 48 |
| Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu | |
| 1 5 10 15 | |
| ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac acc | 96 |
| Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr | |
| 20 25 30 | |
| ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac gtg | 144 |
| Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val | |
| 35 40 45 | |
| agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc gtg | 192 |
| Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val | |
| 50 55 60 | |
| gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac agc | 240 |
| Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser | |
| 65 70 75 | |

acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg ctg 288
 Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
 80 85 90 95

aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca gcc 336
 Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
 100 105 110

ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca 384
 Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
 115 120 125

cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac cag 432
 Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
 130 135 140

gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc gcc 480
 Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 145 150 155

gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc acg 528
 Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 160 165 170 175

cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc 576
 Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 180 185 190

acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc 624
 Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
 195 200 205

gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc 672
 Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 210 215 220

ctg tct ccg ggt aaa ggt gga ggt ggt ggt ttc gaa tgg acc ccg ggt 720
 Leu Ser Pro Gly Lys Gly Gly Gly Gly Gly Phe Glu Trp Thr Pro Gly
 225 230 235

tac tgg cag ccg tac gct ctg ccg ctg taatggatcc ctcgag 763
 Tyr Trp Gln Pro Tyr Ala Leu Pro Leu
 240 245

<210> 1060

<211> 248

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc IL-1
ANTAGONIST

<400> 1060

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Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
  1              5              10              15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
              20              25              30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
              35              40              45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
              50              55              60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
              65              70              75              80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
              85              90              95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
              100              105              110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
              115              120              125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
              130              135              140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
              145              150              155              160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
              165              170              175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
              180              185              190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
              195              200              205

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
              210              215              220

Ser Pro Gly Lys Gly Gly Gly Gly Gly Phe Glu Trp Thr Pro Gly Tyr

```

225

230

235

240

Trp Gln Pro Tyr Ala Leu Pro Leu
245

<210> 1061

<211> 757

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: IL-1 ANTAGONIST
Fc

<220>

<221> CDS

<222> (4)..(747)

<400> 1061

| | |
|---|-----|
| cat atg ttc gaa tgg acc ccg ggt tac tgg cag ccg tac gct ctg ccg | 48 |
| Met Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro Tyr Ala Leu Pro | |
| 1 5 10 15 | |
| ctg ggt gga ggc ggt ggg gac aaa act cac aca tgt cca cct tgc cca | 96 |
| Leu Gly Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro | |
| 20 25 30 | |
| gca cct gaa ctc ctg ggg gga ccg tca gtt ttc ctc ttc ccc cca aaa | 144 |
| Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys | |
| 35 40 45 | |
| ccc aag gac acc ctc atg atc tcc ccg acc cct gag gtc aca tgc gtg | 192 |
| Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val | |
| 50 55 60 | |
| gtg gtg gac gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac | 240 |
| Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr | |
| 65 70 75 | |
| gtg gac ggc gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag | 288 |
| Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu | |
| 80 85 90 95 | |
| cag tac aac agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac | 336 |
| Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His | |
| 100 105 110 | |

cag gac tgg ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa 384
 Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
 115 120 125

gcc ctc cca gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag 432
 Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
 130 135 140

ccc cga gaa cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg 480
 Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
 145 150 155

acc aag aac cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc 528
 Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
 160 165 170 175

agc gac atc gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac 576
 Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
 180 185 190

tac aag acc acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc 624
 Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
 195 200 205

tac agc aag ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc 672
 Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
 210 215 220

ttc tca tgc tcc gtg atg cat gag gct ctg cac aac cac tac acg cag 720
 Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
 225 230 235

aag agc ctc tcc ctg tct ccg ggt aaa taatggatcc 757
 Lys Ser Leu Ser Leu Ser Pro Gly Lys
 240 245

<210> 1062

<211> 248

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:IL-1 ANTAGONIST

Fc

<400> 1062

Met Phe Glu Trp Thr Pro Gly Tyr Trp Gln Pro Tyr Ala Leu Pro Leu
 1 5 10 15

Gly Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
 20 25 30

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
 35 40 45

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
 50 55 60

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
 65 70 75 80

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
 85 90 95

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
 100 105 110

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
 115 120 125

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
 130 135 140

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
 145 150 155 160

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
 165 170 175

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
 180 185 190

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
 195 200 205

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
 210 215 220

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
 225 230 235 240

Ser Leu Ser Leu Ser Pro Gly Lys
 245

<210> 1063
 <211> 773
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-VEGF
 ANTAGONIST

<220>

<221> CDS

<222> (4)..(759)

<400> 1063

| | |
|---|-----|
| cat atg gac aaa act cac aca tgt cca ccg tgc cca gca cct gaa ctc | 48 |
| Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu | |
| 1 5 10 15 | |
| ctg ggg gga ccg tca gtt ttc ctc ttc ccc cca aaa ccc aag gac acc | 96 |
| Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr | |
| 20 25 30 | |
| ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac gtg | 144 |
| Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val | |
| 35 40 45 | |
| agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc gtg | 192 |
| Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val | |
| 50 55 60 | |
| gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac agc | 240 |
| Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser | |
| 65 70 75 | |
| acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg ctg | 288 |
| Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu | |
| 80 85 90 95 | |
| aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca gcc | 336 |
| Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala | |
| 100 105 110 | |
| ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca | 384 |
| Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro | |
| 115 120 125 | |
| cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac cag | 432 |
| Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln | |

| 130 | 135 | 140 | |
|---|-----|-----|-----|
| gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc gcc | | | 480 |
| Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala | | | |
| 145 | 150 | 155 | |
| gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc acg | | | 528 |
| Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr | | | |
| 160 | 165 | 170 | 175 |
| cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc | | | 576 |
| Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu | | | |
| 180 | 185 | 190 | |
| acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc | | | 624 |
| Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser | | | |
| 195 | 200 | 205 | |
| gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc | | | 672 |
| Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser | | | |
| 210 | 215 | 220 | |
| ctg tct ccg ggt aaa ggt ggt ggt ggt ggt gtt gaa ccg aac tgt gac | | | 720 |
| Leu Ser Pro Gly Lys Gly Gly Gly Gly Gly Val Glu Pro Asn Cys Asp | | | |
| 225 | 230 | 235 | |
| atc cat gtt atg tgg gaa tgg gaa tgt ttt gaa cgt ctg taactcgagg | | | 769 |
| Ile His Val Met Trp Glu Trp Glu Cys Phe Glu Arg Leu | | | |
| 240 | 245 | 250 | |
| atcc | | | 773 |

<210> 1064

<211> 252

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc-VEGF
ANTAGONIST

<400> 1064

| |
|---|
| Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu |
| 1 5 10 15 |

| |
|---|
| Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu |
| 20 25 30 |

| |
|---|
| Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser |
|---|

| | | |
|---|-----|-----|
| 35 | 40 | 45 |
| His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu | | |
| 50 | 55 | 60 |
| Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr | | |
| 65 | 70 | 75 |
| Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn | | |
| 85 | 90 | 95 |
| Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro | | |
| 100 | 105 | 110 |
| Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln | | |
| 115 | 120 | 125 |
| Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val | | |
| 130 | 135 | 140 |
| Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val | | |
| 145 | 150 | 155 |
| Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro | | |
| 165 | 170 | 175 |
| Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr | | |
| 180 | 185 | 190 |
| Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val | | |
| 195 | 200 | 205 |
| Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu | | |
| 210 | 215 | 220 |
| Ser Pro Gly Lys Gly Gly Gly Gly Gly Val Glu Pro Asn Cys Asp Ile | | |
| 225 | 230 | 235 |
| His Val Met Trp Glu Trp Glu Cys Phe Glu Arg Leu | | |
| 245 | 250 | |

<210> 1065

<211> 773

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: VEGF ANTAGONIST

Fc

<220>

<221> CDS

<222> (4)..(759)

<400> 1065

| | |
|---|-----|
| cat atg gtt gaa ccg aac tgt gac atc cat gtt atg tgg gaa tgg gaa | 48 |
| Met Val Glu Pro Asn Cys Asp Ile His Val Met Trp Glu Trp Glu | |
| 1 5 10 15 | |
| tgt ttt gaa cgt ctg ggt ggt ggt ggt ggt gac aaa act cac aca tgt | 96 |
| Cys Phe Glu Arg Leu Gly Gly Gly Gly Gly Asp Lys Thr His Thr Cys | |
| 20 25 30 | |
| cca ccg tgc cca gca cct gaa ctc ctg ggg gga ccg tca gtt ttc ctc | 144 |
| Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu | |
| 35 40 45 | |
| ttc ccc cca aaa ccc aag gac acc ctc atg atc tcc cgg acc cct gag | 192 |
| Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu | |
| 50 55 60 | |
| gtc aca tgc gtg gtg gtg gac gtg agc cac gaa gac cct gag gtc aag | 240 |
| Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys | |
| 65 70 75 | |
| ttc aac tgg tac gtg gac ggc gtg gag gtg cat aat gcc aag aca aag | 288 |
| Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys | |
| 80 85 90 95 | |
| ccg cgg gag gag cag tac aac agc acg tac cgt gtg gtc agc gtc ctc | 336 |
| Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu | |
| 100 105 110 | |
| acc gtc ctg cac cag gac tgg ctg aat ggc aag gag tac aag tgc aag | 384 |
| Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys | |
| 115 120 125 | |
| gtc tcc aac aaa gcc ctc cca gcc ccc atc gag aaa acc atc tcc aaa | 432 |
| Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys | |
| 130 135 140 | |
| gcc aaa ggg cag ccc cga gaa cca cag gtg tac acc ctg ccc cca tcc | 480 |
| Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser | |
| 145 150 155 | |

cgg gat gag ctg acc aag aac cag gtc agc ctg acc tgc ctg gtc aaa 528
 Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
 160 165 170 175

 ggc ttc tat ccc agc gac atc gcc gtg gag tgg gag agc aat ggg cag 576
 Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
 180 185 190

 ccg gag aac aac tac aag acc acg cct ccc gtg ctg gac tcc gac ggc 624
 Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
 195 200 205

 tcc ttc ttc ctc tac agc aag ctc acc gtg gac aag agc agg tgg cag 672
 Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
 210 215 220

 cag ggg aac gtc ttc tca tgc tcc gtg atg cat gag gct ctg cac aac 720
 Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
 225 230 235

 cac tac acg cag aag agc ctc tcc ctg tct ccg ggt aaa taactcgagg 769
 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 240 245 250

 atcc 773

<210> 1066

<211> 252

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence: VEGF ANTAGONIST

Fc

<400> 1066

Met Val Glu Pro Asn Cys Asp Ile His Val Met Trp Glu Trp Glu Cys
 1 5 10 15

Phe Glu Arg Leu Gly Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro
 20 25 30

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
 35 40 45

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
 50 55 60

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
 65 70 75 80
 Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
 85 90 95
 Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
 100 105 110
 Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
 115 120 125
 Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
 130 135 140
 Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
 145 150 155 160
 Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
 165 170 175
 Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
 180 185 190
 Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
 195 200 205
 Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
 210 215 220
 Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
 225 230 235 240
 Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 245 250

<210> 1067

<211> 748

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-MMP
 INHIBITOR

<220>

<221> CDS

<222> (4)..(732)

<400> 1067

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|---|-----|
| cat atg gac aaa act cac aca tgt cca cct tgt cca gct ccg gaa ctc | 48 |
| Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu | |
| 1 5 10 15 | |
| ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac acc | 96 |
| Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr | |
| 20 25 30 | |
| ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac gtg | 144 |
| Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val | |
| 35 40 45 | |
| agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc gtg | 192 |
| Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val | |
| 50 55 60 | |
| gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac agc | 240 |
| Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser | |
| 65 70 75 | |
| acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg ctg | 288 |
| Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu | |
| 80 85 90 95 | |
| aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca gcc | 336 |
| Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala | |
| 100 105 110 | |
| ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca | 384 |
| Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro | |
| 115 120 125 | |
| cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac cag | 432 |
| Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln | |
| 130 135 140 | |
| gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc gcc | 480 |
| Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala | |
| 145 150 155 | |
| gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc acg | 528 |
| Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr | |
| 160 165 170 175 | |

cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc 576
 Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 180 185 190

acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc 624
 Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
 195 200 205

gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc 672
 Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 210 215 220

ctg tct ccg ggt aaa ggt gga ggt ggt ggt tgc acc acc cac tgg ggt 720
 Leu Ser Pro Gly Lys Gly Gly Gly Gly Gly Cys Thr Thr His Trp Gly
 225 230 235

ttc acc ctg tgc taatggatcc ctcgag 748
 Phe Thr Leu Cys
 240

<210> 1068

<211> 243

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc-MMP
 INHIBITOR

<400> 1068

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
 1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
 20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
 65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
 85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro

100 105 110
 Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
 115 120 125
 Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
 130 135 140
 Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
 145 150 155 160
 Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
 165 170 175
 Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
 180 185 190
 Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
 195 200 205
 Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
 210 215 220
 Ser Pro Gly Lys Gly Gly Gly Gly Gly Cys Thr Thr His Trp Gly Phe
 225 230 235 240
 Thr Leu Cys

<210> 1069

<211> 763

<212> DNA

<213> Artificial Sequence

<220>

 <223> Description of Artificial Sequence:MMP INHIBITOR
 Fc

<220>

<221> CDS

<222> (4)..(753)

<400> 1069

cat atg tgc acc acc cac tgg ggt ttc acc ctg tgc ggt gga ggc ggt 48
 Met Cys Thr Thr His Trp Gly Phe Thr Leu Cys Gly Gly Gly Gly
 1 5 10 15

| | |
|---|-----|
| ggg gac aaa ggt gga ggc ggt ggg gac aaa act cac aca tgt cca cct | 96 |
| Gly Asp Lys Gly Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro | |
| 20 25 30 | |
| tgc cca gca cct gaa ctc ctg ggg gga ccg tca gtt ttc ctc ttc ccc | 144 |
| Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro | |
| 35 40 45 | |
| cca aaa ccc aag gac acc ctc atg atc tcc cgg acc cct gag gtc aca | 192 |
| Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr | |
| 50 55 60 | |
| tgc gtg gtg gtg gac gtg agc cac gaa gac cct gag gtc aag ttc aac | 240 |
| Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn | |
| 65 70 75 | |
| tgg tac gtg gac ggc gtg gag gtg cat aat gcc aag aca aag ccg cgg | 288 |
| Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg | |
| 80 85 90 95 | |
| gag gag cag tac aac agc acg tac cgt gtg gtc agc gtc ctc acc gtc | 336 |
| Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val | |
| 100 105 110 | |
| ctg cac cag gac tgg ctg aat ggc aag gag tac aag tgc aag gtc tcc | 384 |
| Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser | |
| 115 120 125 | |
| aac aaa gcc ctc cca gcc ccc atc gag aaa acc atc tcc aaa gcc aaa | 432 |
| Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys | |
| 130 135 140 | |
| ggg cag ccc cga gaa cca cag gtg tac acc ctg ccc cca tcc cgg gat | 480 |
| Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp | |
| 145 150 155 | |
| gag ctg acc aag aac cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc | 528 |
| Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe | |
| 160 165 170 175 | |
| tat ccc agc gac atc gcc gtg gag tgg gag agc aat ggg cag ccg gag | 576 |
| Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu | |
| 180 185 190 | |
| aac aac tac aag acc acg cct ccc gtg ctg gac tcc gac ggc tcc ttc | 624 |
| Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe | |
| 195 200 205 | |

ttc ctc tac agc aag ctc acc gtg gac aag agc agg tgg cag cag ggg 672
 Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
 210 215 220

aac gtc ttc tca tgc tcc gtg atg cat gag gct ctg cac aac cac tac 720
 Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
 225 230 235

acg cag aag agc ctc tcc ctg tct ccg ggt aaa taatggatcc 763
 Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 240 245 250

<210> 1070

<211> 250

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:MMP INHIBITOR
 Fc

<400> 1070

Met Cys Thr Thr His Trp Gly Phe Thr Leu Cys Gly Gly Gly Gly Gly
 1 5 10 15

Asp Lys Gly Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys
 20 25 30

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
 35 40 45

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
 50 55 60

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
 65 70 75 80

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
 85 90 95

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
 100 105 110

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
 115 120 125

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
 130 135 140

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
145 150 155 160

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
165 170 175

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
180 185 190

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
195 200 205

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Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
      210                      215                      220

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| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Phe | Ser | Cys | Ser | Val | Met | His | Glu | Ala | Leu | His | Asn | His | Tyr | Thr |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
245 250

<210> 1071

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 1071

Cys Gly Arg Glu Cys Pro Arg Leu Cys Gln Ser Ser Cys
1 5 10

<210> 1072

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 1072

Cys Asn Gly Arg Cys Val Ser Gly Cys Ala Gly Arg Cys
1 5 10

<210> 1073

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 1073

Cys Leu Ser Gly Ser Leu Ser Cys
1 5

<210> 1074

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 1074

Asn Gly Arg Ala His Ala
1 5

<210> 1075

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<220>

<221> CDS

<222> (10)..(189)

<400> 1075

Cys Asn Gly Arg Cys

1 5

<210> 1076

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 1076

Cys Asp Cys Arg Gly Asp Cys Phe Cys

1 5

<210> 1077

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 1077

Cys Gly Ser Leu Val Arg Cys

1 5

<210> 1078

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 1078

Arg Thr Asp Leu Asp Ser Leu Arg

1

5

<210> 1079

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:INTEGRIN
BINDING PEPTIDE

<400> 1079 .

Gly Asp Leu Asp Leu Leu Lys Leu Arg Leu Thr Leu

1

5

10

<210> 1080

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 1080

Gly Asp Leu His Ser Leu Arg Gln Leu Leu Ser Arg

1

5

10

<210> 1081

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 1081

Arg Asp Asp Leu His Met Leu Arg Leu Gln Leu Trp

1

5

10

<210> 1082
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 1082
Ser Ser Asp Leu His Ala Leu Lys Lys Arg Tyr Gly
1 5 10

<210> 1083
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 1083
Arg Gly Asp Leu Lys Gln Leu Ser Glu Leu Thr Trp
1 5 10

<210> 1084
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial
Sequence:INTEGRIN-BINDING PEPTIDE

<400> 1084
Arg Gly Asp Leu Ala Ala Leu Ser Ala Pro Pro Val
1 5 10

<210> 1085
<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ANTAGONIST
PEPTIDE

<400> 1085

Asp Phe Leu Pro His Tyr Lys Asn Thr Ser Leu Gly His Arg Pro
1 5 10 15

<210> 1086

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VEGF ANTAGONIST
PEPTIDE

<400> 1086

Gly Glu Arg Trp Cys Phe Asp Gly Pro Leu Thr Trp Val Cys Gly Glu
1 5 10 15

Glu Ser

<210> 1087

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:VEGF ANTAGONIST
PEPTIDE

<400> 1087

Arg Gly Trp Val Glu Ile Cys Val Ala Asp Asp Asn Gly Met Cys Val
1 5 10 15

Thr Glu Ala Gln
20

<210> 1088
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: VEGF ANTAGONIST
PEPTIDE

<400> 1088
Gly Trp Asp Glu Cys Asp Val Ala Arg Met Trp Glu Trp Glu Cys Phe
1 5 10 15

Ala Gly Val

<210> 1089
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: VEGF ANTAGONIST
PEPTIDE

<400> 1089
Arg Gly Trp Val Glu Ile Cys Glu Ser Asp Val Trp Gly Arg Cys Leu
1 5 10 15

<210> 1090
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: VEGF ANTAGONIST
PEPTIDE

<400> 1090
Arg Gly Trp Val Glu Ile Cys Glu Ser Asp Val Trp Gly Arg Cys Leu
1 5 10 15

<210> 1091
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VEGF ANTAGONIST
PEPTIDE

<400> 1091
Gly Gly Asn Glu Cys Asp Ile Ala Arg Met Trp Glu Trp Glu Cys Phe
1 5 10 15

Glu Arg Leu

<210> 1092
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:VEGF ANTAGONIST
PEPTIDE

<400> 1092
Arg Gly Trp Val Glu Ile Cys Ala Ala Asp Asp Tyr Gly Arg Cys Leu
1 5 10 15

<210> 1093
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MMP INHIBITOR
PEPTIDE

<400> 1093
Cys Leu Arg Ser Gly Xaa Gly Cys
1 5

<210> 1094
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MMP INHIBITOR
PEPTIDE

<400> 1094
Cys Xaa Xaa His Trp Gly Phe Xaa Xaa Cys
1 5 10

<210> 1095
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MMP INHIBITOR
PEPTIDE

<400> 1095
Cys Xaa Pro Xaa Cys
1 5

<210> 1096
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MMP INHIBITOR
PEPTIDE

<400> 1096
Cys Arg Arg His Trp Gly Phe Glu Phe Cys
1 5 10

<210> 1097
<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MMP INHIBITOR
PEPTIDE

<400> 1097

| | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Thr | Thr | His | Trp | Gly | Phe | Thr | Leu | Ser |
| 1 | | | | 5 | | | | | 10 |

<210> 1098

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MMP INHIBITOR
PEPTIDE

<400> 1098

| | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Ser | Leu | His | Trp | Gly | Phe | Trp | Trp | Cys |
| 1 | | | | 5 | | | | | 10 |

<210> 1099

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:CARBOHYDRATE
(GD1 ALPHA) MIMETIC PEPTIDE

<400> 1099

| | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Trp | His | Trp | Arg | His | Arg | Ile | Pro | Leu | Gln | Leu | Ala | Ala | Gly | Arg |
| 1 | | | | 5 | | | | | 10 | | | | | 15 |

<210> 1100

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: BETA-2 GP1AB
BINDING PEPTIDE

<400> 1100

Leu Lys Thr Pro Arg Val
1 5

<210> 1101

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: BETA-2 GP1AB
BINDING PEPTIDE

<400> 1101

Asn Thr Leu Lys Thr Pro Arg Val
1 5

<210> 1102

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: BETA-2 GP1AB
BINDING PROTEIN

<400> 1102

Asn Thr Leu Lys Thr Pro Arg Val Gly Gly Cys
1 5 10

<210> 1103

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: BETA-2 GP1AB
BINDING PROTEIN

<400> 1103

Lys Asp Lys Ala Thr Phe

1

5

<210> 1104

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: BETA-1 GP1AB
BINDING PROTEIN

<400> 1104

Lys Asp Lys Ala Thr Phe Gly Cys His Asp

1

5

10

<210> 1105

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: BETA-2 GP1AB
BINDING PEPTIDE

<400> 1105

Lys Asp Lys Ala Thr Phe Gly Cys His Asp Gly Cys

1

5

10

<210> 1106

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: BETA-2 GP1AB
BINDING PROTEIN

<400> 1106

Thr Leu Arg Val Tyr Lys

1

5

<210> 1107

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: BETA-2 GP1AB
BINDING PROTEIN

<400> 1107

Ala Thr Leu Arg Val Tyr Lys Gly Gly

1

5

<210> 1108

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: BETA-2 GP1AB
BINDING PROTEIN

<400> 1108

Cys Ala Thr Leu Arg Val Tyr Lys Gly Gly

1

5

10

<210> 1109

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: MEMBRANE
TRANSPORTING PEPTIDE

<400> 1109

Ile Asn Leu Lys Ala Leu Ala Ala Leu Ala Lys Lys Ile Leu

1

5

10

<210> 1110
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MEMBRANE
TRANSPORTING PEPTIDE

<400> 1110
Gly Trp Thr Leu Asn Ser Ala Gly Tyr Leu Leu Gly
1 5 10

<210> 1111
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:MEMBRANE
TRANSPORTING PEPTIDE

<400> 1111
Gly Trp Thr Leu Asn Ser Ala Gly Tyr Leu Leu Gly Lys Ile Asn Leu
1 5 10 15

Lys Ala Leu Ala Ala Leu Ala Lys Lys Ile Leu
20 25

<210> 1112
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:FC PCR PRIMER

<400> 1112
aacataagta cctgtaggat cg 22

<210> 1113
<211> 81

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TNF ALPHA
PCR PRIMER

<220>

<221> CDS

<222> (1)..(126)

<400> 1113

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| ccg | cgg | atc | cat | tac | gga | cgg | tga | ccc | aga | gag | gtg | ttt | ttg | tag | tgc | 48 |
| Pro | Arg | Ile | His | Tyr | Gly | Arg | | Pro | Arg | Glu | Val | Phe | Leu | | Cys | |
| 1 | | | | | 5 | | | 10 | | | | | 15 | | | |
| | | | | | | | | | | | | | | | | |
| ggc | agg | aag | tca | cca | cca | cct | cca | cct | tta | ccc | | | | | | 81 |
| Gly | Arg | Lys | Ser | Pro | Pro | Pro | Pro | Pro | Leu | Pro | | | | | | |
| | | | 20 | | | | | 25 | | | | | | | | |

<210> 1114

<211> 7

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc-TNF ALPHA
PCR PRIMER

<400> 1114

| | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|
| Pro | Arg | Ile | His | Tyr | Gly | Arg |
| 1 | | | | | 5 | |

<210> 1115

<211> 6

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc-TNF ALPHA
PCR PRIMER

<400> 1115

| | | | | | |
|-----|-----|-----|-----|-----|-----|
| Pro | Arg | Glu | Val | Phe | Leu |
| 1 | | | | 5 | |

<210> 1116

<211> 12

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence:Fc-TNF ALPHA
PCR PRIMER

<400> 1116

Cys Gly Arg Lys Ser Pro Pro Pro Pro Pro Leu Pro
1 5 10

<210> 1117

<211> 81

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:TNF-ALPHA
INHIBITOR-Fc PCR PRIMER

<400> 1117

gaataacata tggacttcct gccgcactac aaaaacacct ctctgggtca ccgtccgggt 60
ggaggcgggtg gggacaaaac t 81

<210> 1118

<211> 81

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
PCR PRIMER

<400> 1118

ccgcggatcc attacagcgg cagagcgtac ggctgccagt aaccgggggt ccattcgaaa 60
ccaccacctc cacctttacc c 81

<210> 1119

<211> 81

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:IL-1 ANTAGONIST
-Fc PCR PRIMER

<400> 1119

gaataacata tgttcgaatg gaccccggt tactggcagc cgtacgctct gccgctgggt 60
ggaggcgggtg gggacaaaac t 81

<210> 1120
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Fc-VEGF
ANTAGONIST OLIGONUCLEOTIDE

<400> 1120
gttgaaccga actgtgacat ccatgttatg tgggaatggg aatgttttga acgtctg 57

<210> 1121
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Fc-VEGF
ANTAGONIST OLIGONUCLEOTIDE

<400> 1121
cagacgttca aaacattccc attcccacat aacatggatg tcacagttcg gttcaac 57

<210> 1122
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Fc-VEGF
ANTAGONIST PCR TEMPLATE

<400> 1122
gttgaaccga actgtgacat ccatgttatg tgggaatggg aatgttttga acgtctg 57

<210> 1123
<211> 48
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc PRIMER

<400> 1123

atttgattct agaaggagga ataacatatg gacaaaactc acacatgt

48

<210> 1124

<211> 51

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc PRIMER

<400> 1124

gtcacagttc gggtcaacac caccaccacc acctttaccc ggagacaggg a

51

<210> 1125

<211> 54

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-VEGF
ANTAGONIST PCR PRIMER

<400> 1125

tccctgtctc cgggtaaagg tggtggtggt ggtggtgaac cgaactgtga catc

54

<210> 1126

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-VEGF
ANTAGONIST-Fc PCR PRIMER

<400> 1126

ccgcggatcc tcgagttaca gacgttcaaa acattccca

39

<210> 1127

<211> 48

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-VEGF
ANTAGONIST-Fc PCR PRIMER

<400> 1127

atttgattct agaaggagga ataacatatg gttgaaccga actgtgac

48

<210> 1128

<211> 51

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-VEGF
ANTAGONIST-Fc PCR PRIMER

<400> 1128

acatgtgtga gttttgtcac caccaccacc acccagacgt tcaaaacatt c

51

<210> 1129

<211> 51

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-PCR PRIMER

<400> 1129

gaatgttttg aacgtctggg tgggtggtggt ggtgacaaaa ctcacacatg t

51

<210> 1130

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc PCR PRIMER

<400> 1130

ccgcgatcc tcgagttatt taccgcgaga cagggagag

39

<210> 1131

<211> 66
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-MMP
INHIBITOR PCR PRIMER

<400> 1131
ccgcggatcc attagcacag ggtgaaaccc cagtgggtgg tgcaaccacc acctccacct 60
ttaccc 66

<210> 1132
<211> 63
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:MMP
INHIBITOR-Fc PCR PRIMER

<400> 1132
gaataacata tgtgcaccac ccactggggt ttcaccctgt gcggtggagg cggtggggac. 60
aaa 63

<210> 1133
<211> 20
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Fc-TMP

<400> 1133
Lys Gly Gly Gly Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu
1 5 10 15
Ala Ala Arg Ala
20